THE GASTRIC DIGESTION OF THE PREMATURE INFANT.

THESIS

Presented for the Degree of
Doctor of Medicine
of the
University of Edinburgh

by

ROBERT ALEXANDER MILLER,
M.A.Cantab., M.B.Ch.B., M.R.C.P.Edin.

April 1939.

CONTENTS.

PREFACE.

At the present day the premature infant mortality rate is approximately fifty per cent, and improvement in prophylactic measures for the maintenance of good health are urgently sought. Paediatricians realise the importance of rational feeding for these frail and delicate infants and have consequently tried countless feeds to improve the prognosis. There is, however, no recognised feed generally accepted, presumably because the patient's response to a specified feed differs from case to case. The various factors responsible for this are not all fully known, and it is hoped that the investigations on the gastric acidity and histology may help to clarify some of the difficulties at present encountered.

I now wish to thank the many friends to whom I am deeply indebted for the accumulation of knowledge for this thesis.

It is with the greatest pleasure I thank Professor /

Professor Charles McNeil for his help and guidance during the many months I have studied children in Edinburgh. It is through him that I have been able to appreciate the work and commence this branch of research which I hope I shall be able to continue in the future. I also wish to thank Miss McGregor of the Royal Hospital for Sick Children, Edinburgh, for her valuable advice in microscopical interpretations and pathological studies. I am indebted to Dr. C. P. Stewart of the Royal Infirmary, Edinburgh, for assistance in biochemistry.

In addition, I am extremely grateful for the Laboratory Assistant's aid without which my work could not have been completed with such ease and efficiency.

I have to thank Professor Johnstone, Dr. Martin and Dr. MacKay for permission to work in the Royal Maternity Hospital and in the Elsie Inglis Hospital, Edinburgh; also Dr. T.Y. Finlay of the Public Health Department for access to the records of infants attending the Infant Welfare Centres, Edinburgh.

Last, but by no means least, my grateful thanks are due to Sister Taylor, Sister Neish and Acting Sister, Ward 2, the Royal Maternity Hospital for obtaining the specimens for me during their arduous duties.

CHAPTER I.

THE DEFINITION OF THE PREMATURE INFANT.

In the past prematurity was based on a group of factors, e.g., the number of weeks gestation, and the length, weight and general development of the infant at birth. Thus, the paediatrician was left to use his own discretion as to the most important factor in determining the diagnosis. For example, Kerr et alia (1936), believed that the method of diagnosis of prematurity based on the length of the foetus at different months of gestation was somewhat rough and ready, but was sufficiently useful for ordinary purposes. Other people would diagnose a baby as premature if it was born before the expected date of delivery.

In 1937 the International paediatric Conference decided that the definition was unsatisfactory both for diagnosis and for statistical and research purposes, thus a new definition was laid down. It states that any infant born weighing 5½ lbs. or less must be considered premature irrespective of any other qualification. This /

This definition, however, is not foo-proof, for it has been said that a newborn infant of seven months gestation has been born weighing 6 lbs., while a mature infant has been born weighing 4lbs. at birth. (Tow 1937). The present definition is also defective in some instances where twins are born; e.g., one twin may weigh over 5½ lbs. while the other may weigh less than 5½ lbs. Although there are these drawbacks to the latest definition there are assets, in that it provides a fairly accurate guide to treatment and prognosis in infancy.

Before commencing this paper it should be remembered that the references, which are quoted, may be most misleading, except for that of Tow's,* as they are all based on the old definition of prematurity. This is evident when it is realised that fifty per cent of the originally premature infants are now classified as mature infants. Statistics of the birth rate of premature infants and their mortality during the first few weeks of their life in the Royal Maternity Hospital, Edinburgh, in the years 1934 and 1938 will demonstrate this point:-

Year. /

* and Spence I938.

	Year.	No. of Prems.	No. of Deaths.	M. R.	Per cent of Deaths in Hospital.
By old definition.	1934	340	109	32%	32
By new definition.	1938	176	70	40%	40

? Diff not Significant Statistica

100%

"

341

175

CHAPTER II.

A REVIEW OF DIGESTIVE FERMENTS WITH SPECIAL REFERENCE TO GASTRIC ACIDITY.

The digestion of the infant is a complex mechanism. It is carried out by means of ferments which are controlled by exogenous and endogenous factors. In healthy children the gastric secretion is mainly due to a reflex nervous mechanism determined through the vagus nerve by stimulation of the mucous membrane of the mouth or by a conditioned reflex involving the higher parts of the brain. A less important factor depends on the extraction from the pyloric mucous membrane of histamine or some related hormone which acts as a chemical messenger to all parts of the stomach. This results in a continual secretion of gastric juice long after reflex effects of feeding have disappeared. (Starling 1936). In disease gastric secreting mechanism is upset as will be shown later.

A review of the literature on the pancreatic and intestinal ferments in infancy as well as on the gastric /

gastric ferments will now be given, for it is impossible to fully appreciate the gastric digestion without taking into account all digestive processes.

PANCREATIC AND INTESTINAL FERMENTS.

The Carbohydrate Ferments.

(1). Lactase is found in the small intestinal contents, the stools, and the intestinal mucosa. It is, however, frequently absent from the intestinal tract of the premature infant as it makes its appearance rather late in foetal life. It is also rarely found in the stools of the newborn. (Nothmann 1909). The relatively large amounts of lactose in milk feeds probably increases the quantity and the activity of lactase. (Hess 1923). The lack of milk sugar fermentation at birth is further indicated by the finding of lactose in the urine of newborn infants.

(2). Invertase is present in embryonal life. It has been found in the intestinal wall and in meconium but there is no use for it in those fed on human milk, or where lactose is used in artificial feeds. (Hess 1923).

(3). Maltase is present in all parts of the intestinal /

intestinal contents of the premature infant. (Ibrahim 1910).

(4). Diastase and Ptyalin. These substances digest starch, and for this reason the latter, although not a pancreatic or intestinal ferment, has been mentioned. Ptyalin is found in the parotid and maxillary secretions even in the premature infant. (Zweifel 1874 and Ibrahim 1910). Diastase is present in the salivary glands, and in the pancreas of the newborn. Ibrahim believes that the pancreatic function, especially of the premature infant, is below that of older infants.

Fat Splitting Ferments.

(1). Lipase is probably present in relatively small quantities in the intestinal tract. (Hess 1923).

The Protein Ferments.

(1). Trypsin is present in the pancreatic extract of the newborn. Ibrahim (1910) found trypsinogen as early as the sixth month of foetal life, while enterokinase has been found in extracts of intestinal mucosa of premature infants.

(2). Erepsin has been demonstrated in the premature child by Langsteinin (1908), Jaeggis (1907), Cohnheim (1903).

Secretin /

Secretin has been found in the small intestine of the newborn full term infant. (Ibrahim and Gross 1908).

The Gastric Ferments.

(1). Lipase is very active in the gastric mucosa of the premature infant. (Hess 1923). In the premature breast fed infant the gastric lipase varied from day to day. (Denes Von Moritz et alia 1923). In children ranging from 6 months to 2 years who were given a test meal of milk and water, 1-3, the gastric lipase was not present in amounts proportional to the free hydrochloric acid. (Giamm 1934).

(2). Rennin secretion varies in amount. It shows a corresponding increase or decrease according to whether the free hydrochloric acid rises or falls.

(3). Pepsin is present in the gastric mucosa as early as the sixth foetal month, though not in such quantities as in older children. It increases in amount up to the third month of life, and then remains at that level. (Hess 1923). The peptic activity follows that of the free hydrochloric acid in the gastric juice, but protein digestion is thought /

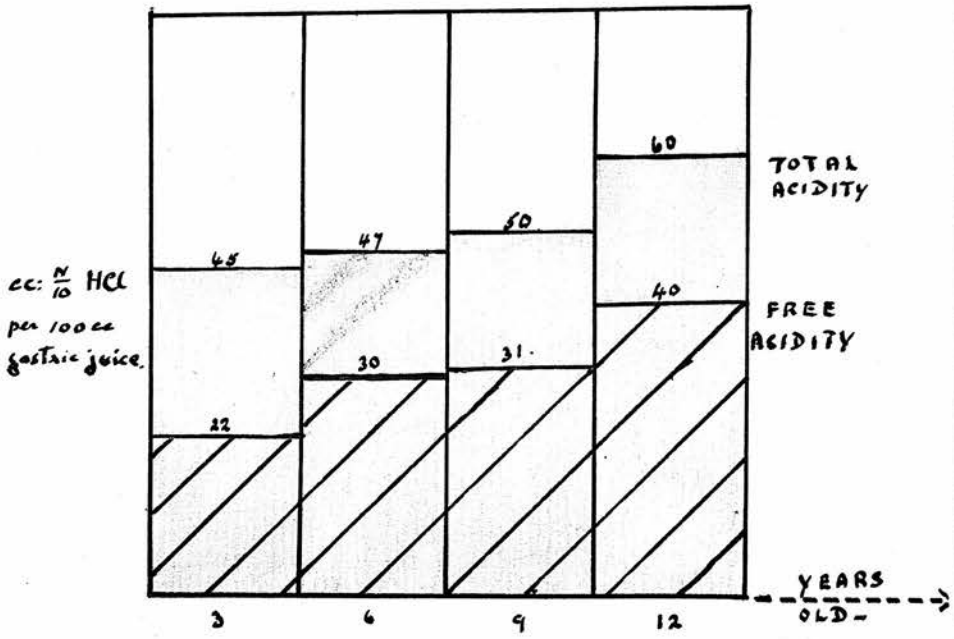
thought to be more an intestinal function between the ages of 1-2, than in younger or older children. (Giamm 1934).

(4). Acidity of the gastric juice of the foetus, infant and child has not been standardised in any way, so that only an impression of the general tendency for the acidity to increase with age can be given by the following references:-

A. Gastric acidity in children over one year.

Ogilvie (1934), after examining 60 healthy and 60 rheumatic fever patients, concluded that the free and total acid increased with age. The pH and the chlorine content of the fasting juice also increased with age. Giamm (1934) also examined the fasting juice and stomach content after a test meal of milk and water, dilution 1-3, and found that the fasting juice was less in quantity than in adults, and that free hydrochloric acid was present in most cases. Parks Faber (1937) said that evidence goes to show that achlorhydria is probably never present in the healthy child. MacFate (1937) believed that the younger the child was the smaller the quantity and degree of acid it secreted. After the first year of life gastric acidity increases in amount until it approaches /

approaches adult values between ages 5-7 years. He gives Ogilvie's table to demonstrate this fact:-



These are only average values, and it is very difficult to draw conclusions - particularly in the lower age limits.

B. <u>The gastric acidity in children under 1 year</u>.

Will and Paterson (1926) found that most infants of this age had free hydrochloric acid in their gastric juice, and that under-weight children had a lower acidity than normal.

Muller <u>et alia</u> (1928) gave 125 c.c. barley water to a series of infants from which they removed the gastric contents after 25 minutes. The free hydrochloric /

hydrochloric acid content was nine units and total acid was twenty units. These values were definitely lower than those for older children.

Tomotake Izumita (1930) carried out a series of test meals on the newborn and older infants. The fifty-two newborn and thirty-five older infants were given 80 c.c. of a solution containing o.3 per cent wheat flour and 2.0 per cent cane sugar. He came to the conclusion that:-

1. Free acidity was 0-18 units and the average was 6 units.
2. Total acidity was 4-26 units with an average of 3-12 units.
3. The pH 2.0-4.2 but in the newborn the pH values were less than in the older infants.
4. The Gunzberg Reaction was positive in 84% and free hydrochloric absent in 14%.

This is admirable work in that it is the first time standard limits of gastric acidity in infancy has been published. The results are probably fairly accurate in spite of the fact that the test meal was not ideal.

Steimann (1936) noticed the gastric acidity to increase during the first year of life.

C. /

C. The Acidity in the Unfed or the Newborn.

Sizyelbowsky (1892) published the first record of an unfed infant having free hydrochloric acid present in its gastric secretion.

Tange (1906) gave the pH of the gastric contents of the unfed as 1.3-1.8. This would mean that Topfer's Reagent would become orange or red, and under such circumstances free hydrochloric is generally present.

Hess and Ibid (1913) tested the gastric secretion of fifty-five unfed infants with congo red and phenolphthalein as indicators and concluded that free hydrochloric acid was present in every case except one. This statement, however, is not justifiable as these indicators are not specific for any particular acid. Secondly, congo red indicates acid at pH5 and Topfer's Reagent at pH4, therefore since Topfer's Reagent does not necessarily prove the presence of hydrochloric acid, congo red will be even less reliable.

Pollitzer (1921) agreed with Hess after testing the gastric contents of a hundred unfed infants.

Negresco and Heresco (1921) emphatically stated that free hydrochloric acid does not appear until the sixth day after birth.

Griswald /

Griswald and Schohl (1925) stated that the gastric secretion of the newborn was well on the acid side of neutral.

D. The gastric acidity of the premature infant.

Denes Von Moritz (1923) published the only work done on this class of infant. The infants he examined were breast fed, and their gastric acidity varied from pH 3.4-6.8. This would mean that all the specimens with a pH below 4 would be alkaline to Topfer's Reagent, and that the corresponding number would, in all probability, contain no hydrochloric acid. The author also found that other tests for gastric function varied widely from day to day.

The validity of the results must be doubted for the milk feeds will produce an abnormally low acidity, and the selected cases would include premature infants weighing up to possibly 7½ lbs.

E. The Gastric Acidity in Foetal Life.

Hess (1923) stated that hydrochloric acid and renin are both present.

Factors influencing Gastric Acidity.

1. Maturity and Age.

The gastric secretion is feeble in the immature infant, /

infant, while in older infants it progressively increases. (Davidson 1921, Klupp et alia 1930, Babbot et alia 1923, and Tomotake 1930).

2. Sex.

In infancy, boys have a greater acid secretion than that of girls. (Tomotake 1930).

3. Constitution. (Davidson 1921).

The acidity of the gastric juice is increased to above normal by persistent vomiting. (Will and Paterson 1926). On the other hand, it is diminished by anaemia (Alice Stewart 1937), and she emphasises the fact that the achlorhydria does not precede the illness, nor does it persist after the anaemia has been cured. Similarly, with severe infections in which there is a systemic disturbance gastric secretion is also affected, but the hypochlorhydria or achlorhydria that develops is only temporary. (Parsons 1929). With marasmus the gastric secretion is diminished. (Parsons 1924).

4. Food.

The continual stimulation of the alimentary tract by food results in a material increase in both quantity and quality of the secretions, particularly in the premature infant provided it possesses a sufficient /

sufficient degree of vitality. (Hess 1923). This view is flatly contradicted by Will and Paterson (1926), and Babbott et alia (1923) who believed that previous feeding has no effect. The former said that the secretion depends upon the general condition of the child.

5. Motility and rate of stomach emptying.

This is greatest when the gastric acidity is highest and is least when the acidity is lowest. (Davidson 1921).

6. Difficulty in swallowing the stomach tube.

It has been shown that when adults swallow the stomach tube it results in a different secretory response, due, presumably, to certain nervous influences, (Bennett and Ryle 1921), but this factor may be neglected when obtaining the gastric residue of the newborn.

Summary of the Digestive Ferments.

1. All the ferments necessary for the digestion of food in mature infants and older children are normally present. In premature infants, however, the lactase is sometimes deficient in quality or in quantity, or in both these respects.

2. /

2. Gastric Acidity.

(A). In children over one year. If the child is healthy acid is always present, and the acidity increases with age.

(B). Infants under one year. Gunzberg's reaction is positive in 84 per cent of cases. Free acidity 0-18 units with an average of 6. The total acidity 4-26 with an average of 3-12 units.

(C). In the unfed infant. Most authors believe that hydrochloric acid is always present, but no estimations of the free and total acidity are available.

(D). The fed and unfed premature infants. Investigations on the pH of the fed infants are unreliable, while the Gunzberg reaction, free acidity and total acidity have not been recorded in either the fed or unfed infants.

3. Factors influencing the gastric digestion.

These include maturity, sex, age, constitution, diet and motility of the stomach.

CHAPTER III.

INVESTIGATIONS ON GASTRIC ACIDITY OF THE UNFED NEWBORN INFANT.

The investigations on quantitative estimations of free and total acidity in the mature and immature newly born infant have never been recorded. In addition, the pH and the frequency with which hydrochloric acid occurs in the unfed premature infant is unknown.

The methods of investigating gastric acidity are numerous but most of them are unreliable. The method of choice, the histamine test, is unpracticable for the newborn infant. The test meals which have been given to children are :-

1. Milk or Milk and Water. The latter was used by Giamm (1934), but this gives fallacious results. Davidson (1928) showed that infants' gastric acidity varied with the buffer action of the milk, and that milk had a particularly high buffer action which lowers the gastric acidity. In fact, Harrison (1937) does not approve of milk being used in any gastric test meal.

2. Barley Water. Muller (1928). This would be preferable /

preferable to milk as its buffer action is slight, but, on the other hand, its stimulating effect on the gastric secretion would be feeble.

3. Sugar and Wheat Flour. This was employed by Tomotake (1930) and has the disadvatage that maximum stimulation of the secretion cannot be produced.

4. The Alcohol Meal. This, consisting of 40 c.c. of seven per cent alcohol, is one of the best types for use in infants. It gives a free hydrochloric acid equivalent of 65 c.c. $\frac{N}{10}$ sodium hydroxide as compared with 29 c.c. with the Ewalds Test meal, and 110 c.c. with the histamine test. (Neale et alia 1931). In the past, the youngest recorded case to have such a meal was eight months old and, therefore, it is unknown whether a fractional meal is possible in the newborn owing to the difficulty of obtaining specimens. Even if it were possible, such a procedure seems unjustifiable in the frail premature infant.

5. The Ewalds meal is totally unsuitable for the infant on account of its powerful buffer action. Apart from this, the response of the gastric secretion to the meal is less than half that which is produced /

produced by an alcohol test.

6. The histamine meal is the only reliable method of estimating the gastric acidity because of its extremely powerful stimulating action as has already been shown by the comparative figures with the alcohol meal. The youngest child reported to have had such a meal was aged two. The dose was 0.15 m.g. (Alice Stewart 1937). Thus, one hesitates to adopt this method for the frail immature infant because the test affects both the nervous and circulatory systems. Besides, Harrison (1937) does not consider the histamine test should be used on patients with a blood pressure below 110 mm. mercury.

7. The fasting juice. This has been used for determining the gastric acidity in the newborn. It is presumably the safest and most reliable method at this age, as it has been universally adopted. The results which are obtained are only approximate values, and the maximum secretion cannot be guaranteed in each individual case. For comparative purposes of the mature and immature infant's power of gastric secretion the method is admirable.

The Validity of a Single Gastric Analysis.

Wheeler (1921) and White (1922) suggested that the /

the analysis of gastric contents formed only a rough method of estimating gastric secretory function. Kopeloff (1922) and Friedenwald et alia (1924) were more optimistic regarding the value of the test. The former considered that there was a similarity in all specimens removed in rapid succession, and if the position of the tube was constant during a test meal, a characteristic curve would be obtained. Friedenwald agreed with this provided the tip of the tube was in the pyloric antrum, or at least beyond the fundus of the stomach. Bennett and Ryle (1921) found that the test meal curve for acidity in the same individual was remarkably constant, but Lyon et alia (1921) did not agree with this view. Bell McAdam (1923) tested one individual on twenty successive days and obtained a very constant result, while A.L. Bloomfield and C.S. Keefer (1924), using histamine as the acid stimulant for the tests, concluded that the response of a person's gastric acidity was as characteristic as his finger-prints. This certainly would not apply to the acidity response with regard to the usual test meal. Vanzant et alia (1931) studied the test meal results from two normal women /

women over a period of several months and found that a single test might be misleading. There was usually no marked variation from day to day, but one woman showed a considerable fluctuation at one period of the test. This coincided with an attack of considerable emotional stress. Hellebrandt et alia (1935) investigated three cases on eight to twenty-one occasions, using histamine and alcohol as stimulants. They concluded that the secretion of the stomach is highly variable in the normal subject because the acid secretion is affected via motor, mechanical, chemical, muscular, humoral and reflex paths, which is beyond satisfactory control. Changes in the physical fitness and general condition of the patient also affect the acidity response. Therefore, a test meal is not a valid procedure. Nevertheless, although the capacity response varied somewhat during the period which their patients were tested, the variation did not at any time exceed ten clinical units on either side of the average for each individual.

The Technique of obtaining Specimens.

The specimens in most cases were taken 6-8 hours after birth, that is, just before they were put to the breast /

breast for the first time. The procedure was to pass a sterile nasal catheter smeared with glycerine into the stomach of the infant. Suction was then gently applied to the tube by the means of a 5 c.c. syringe in order to withdraw the stomach contents. The specimen was then placed in a sterile test tube and corked. It was then tested within 6 hours of being taken. If this rule was not adhered to it was found that the acidity varied from time to time. For example, specimens which contained hydrochloric acid tended to become more acid on standing, while those that had no "free" acid altered very little. An explanation of this phenomenon is not known, but the following suggestions have been made:-

1. Bacterial fermentation as a cause of increasing acidity is not satisfactory, for bacteria do not grow readily in an acid medium. However, bacteria in the alkaline specimens could explain alterations in acidity, particularly since it is possible for acid resisting bacterial spores to be present in the juice. (La Mott)

2. Hanks (1926) suggests the interaction of acid with some enzyme present in the juice as a cause for alterations /

alterations in acidity.

Tests performed on the Gastric Juice of the unfed infant.

1. The macroscopic appearance and volume were noted. This is of value in detecting blood and bile in certain cases, and the necessary biochemical test can be carried out. Bile being detected by means of Heller's Test, that is, the juice is added to concentrated nitric acid and if bile is present a green ring appears at the junction of the two fluids. For blood the standard Benzidine Test was used. The volume is interesting as it seems to bear some relation to the degree of acidity.

2. The pH by means of indicators was recorded.

Topfer's Reagent .....3-4 when colour changes.

Congo Red 3-5

Phenolphthalein 8-10

3. Gunzberg Reaction is specific for hydrochloric acid, and is essential for its detection. If pH is first estimated the presence or absence of the hydrochloric acid can be forecast correctly in about 94-95 percent of cases.

4. /

4. Quantitative estimation of free and total acidity. In all cases where 0.2 c.c. juice was present it was used for titration with $\frac{N}{10}$ sodium hydroxide. The end point for "free" acidity was taken when Topfer's Reagent turned yellow, while the end point of the titration for total acidity was when phenolphthalein turned pink.

5. Microscopic examination of the secretion. One or two slides were made of each specimen. One was stained with Leishmann, the other with Gram. They were then examined for Bacteria and Liquor Amnii.

The diagnosis of liquor amnii is not easy, therefore its appearance will be described. It contains epidermal scales, sebacious matter, and, in some instances, it may be contaminated with meconium or blood. Meconium has the same microscopical appearance as liquor amnii. In practice the characteristics of the epidermal scales have to be relied on for the diagnosis. The scales are degenerated squamous cells, the oldest of which appear like twisted structureless non-nucleated fibrils, while the less degenerated are polygonal in outline. Their cytoplasm is stained uniformly, and as a rule they have no nucleus. Rarely, however, an /

an occasional nucleated squamous cell is present. These are liable to be confused with the squamous cells of the mouth or oesophagus which frequently contaminate the specimen during the passing of the catheter. They may be differentiated by the fact that the nucleated cells of liquor amnii form only a very small proportion of the total cells present.

Fallacies and Errors in Estimating Acidity.

To fully appreciate the value of the results on gastric acidity it is essential to take into account all sources of error that may arise, apart from variations that may occur from factors controlling and influencing the gastric secretion.

1. Micro-estimations. When these results are expressed as a per centage any error will be magnified five hundred times.

2. The end point of the titrations is not sharp, and, therefore, can give rise to incorrect readings on the burette. Fortunately, however, all the titrations were carried out by one person under similar circumstances, and a series of controls on mature /

mature babies were done so that discrepancies in the results and conclusions would be at a minimum.

3. The secretion is an unhomogeneous mass as pointed out by Gorham (1921).

4. The presence of bile in the gastric juice of the healthy infant is thought to occur by some authorities, while others disagree (Stewart and Dunlop 1937). In the investigations bile was detected in some of the samples and this was due to either regurgitation of bile into the stomach or to the stomach-tube passing into the duodenum. The presence in the juice would result in the acidity being reduced by the alkaline bile.

5. The contamination by blood of the gastric juice occurs either through local injury to the mouth, oesophagus or stomach, or by swallowing blood from the birth passages. Its protein content will act as a buffer to the gastric secretion and reduce its acidity.

6. The swallowing of saliva or mucus. Its action on the gastric contents has been a subject of dispute as to what extent it alters the acidity. The specimens generally contain mucus and saliva and, as a rule, they account for a large proportion of the /

the total quantity, therefore they must have a diluting effect, even if they do not possess power to neutralise acid. Bell (1923) considered that saliva and mucus have only a minor effect on the acidity of the secretions.

7. Liquor amnii is sometimes swallowed by the foetus, (Johnstone 1937) and, owing to its alkaline properties, it will neutralise the acids in the stomach.

8. The bacteria in the stomach contents of the new-born, or within 8 hours of birth would seem improbable but having found specimens with bacteria the literature on the subject was examined. All the available help in this line was grouped under the bacterial invasion of the mouth, pharynx, and intestine in the newborn. References on the bacterial flora of the stomach in the newborn were conspicuously absent.

Bacteria of the Mouth and Pharynx in the New Born.

Salmon (1922-23) reviewed the literature on this subject. He quoted Kneise who found organisms present in 97 per cent of infants immediately after birth. /

birth. On the other hand, Kestlin reported the mouth to be sterile, but Salmon disagreed with him. Schweitzer found organisms present in 46 per cent of cases, which compared favourably with 47 per cent given by the author.

Kneeland (1930) investigated the upper respiratory flora of 30 newborn infants by taking swabs from the nose and pharynx. The first culture taken on delivery in the delivery-room, he found almost invariably to be sterile. The pharynx was usually sterile until after the first feed. In the nose 80 per cent were sterile on the first day and 40 per cent on the second day.

Gundel and Schwartz (1931-32) made 1137 examinations on fifty-two babies, fifty-one mothers and twelve attendants. He found that flora of the babies' mouths, in the majority of cases, was sterile during the first 12 hours of life. The first organisms to appear were "banal", especially the staphylococcus albus, mouth streptococcus, micrococcus catarrhalis and b. coli. From the sixth to the twenty-fourth hour of life thirty-three out of fifty-two were sterile.

Muller and Bater (1934) were interested in pneumonia /

pneumonia of the newborn, and in their research they took mouth and nose swabs of twenty-five children at birth, and after 6, 12, 24 and 72 hours. In more than half the spontaneously born children immediately after birth there was a more or less rich flora.

Intestinal Flora of the Newborn.

Breslau (1866) was the first to show that the intestinal tract of the newborn infant was invaded by bacteria often within ten hours after birth. He presumed the infection to be either an ascending or a descending one. Billroth (1874) confirmed Breslau's findings. Nothagel (1881) agreed with his predecessors. Escherich (1885) came to the same conclusions, and in 1886 he showed that in some cases, even when bacteria were not demonstable microscopically, their presence could be shown culturally as early as the fourth hour. The first invaders were tetradencocci and kettencocci, and that, while the flora of the first day was simple, that of the second day was more complex, often containing in addition to bacillus coli and bacillus aerogenes, bacillus subtilis and other sporulating bacilli and yeasts. This variable flora gave way about the fourth day when /

when the dark meconium was replaced by yellow stools which were acid and mucoid, to a flora in which slender granular gram positive and non-sporulating rods greatly predominated. Many workers (1900) have since noted bacillus acidophilus present in the healthy intestine at all ages. Naujoks (1921) showed that the majority of pregnant women harbour bacillus acidophilus in the vaginal secretions, so practically every infant acquires it at birth.

Hall and O'Toole (1935) made an intensive study of sixty-three specimens of meconium and faeces secured from ten newborn infants during the first ten days of life. Seven infants passed sterile specimens on the first day of life, but by the second day all the infants passed specimens containing bacteria. At least five genera and eighteen species were present. These included streptococci and micrococci, bacillus coli, bacillus aerogenes, lactobacillus bifidus and acidophilus, hay bacillus and anaerobic bacilli.

Pfaundler and Schlossmann (1935) found that the bacteria which reach the stomach in the food, in particular the bacilli of the colon group which are so common in cow's milk are killed by the gastric hydrochloric acid. (Pathogenic bacteria are not included). They can almost always be demonstrated in /

in the gastric contents during the first hours after the ingestion of food although only in small quantities, but with the increasing acidity during the latter stages of digestion and in the intervals between the feeds the sterilizing effect of the higher degrees of acidity (about pH 3.7) is more and more strongly manifest. No importance need be ascribed to the transient occurrence of bacteria in the gastric contents after the ingestion of food, since there is no possibility for them proliferating in the stomach, or to affect the digestive processes, or to decompose the constituents of the food. Therefore we may conclude that numerous forms of cocci and bacilli are likely to invade the stomach contents within a few hours of birth. Also, they will survive or even proliferate if the gastric acidity is low enough. Lastly, the identification of the organisms is beyond the scope of this paper.

Standards for normal "Free" and "Total" Gastric Acidity.

In order to discuss gastric acidity it is necessary to fix a standard of normal. As such a standard does not exist in infancy or childhood an "adult" one will have to be adopted.

Normal "Free" acidity in adults. Bennet and Ryle (1921) studied very carefully a hundred males from this point of view and their charts show the wide limits of "free" acidity. This is probably as good a guide as we possess to what we may consider normal in the adult. Twenty-two units* was the maximum in the fasting juice and forty-six units after the test meal. Vanzant et alia (1932) studied the normal range of gastric acidity in 3767 cases, varying from adolescence to old age. The patients were given an Ewald Test Meal and the adult healthy male had 45-50 clinical units of "free" acidity, the adult female 35 units, and, in the aged males, 30-35 units. Sagal et alia (1933) even in a larger series of cases obtained similar results. Pierce et alia (1931) and Polland et alia (1932) used histamine or alcohol test meals to show the wide variations in the normal individual, and the impossibility of setting well defined /

* I unit = I cc: $\frac{N}{10}$ HCl per 100cc: gastric juice.

defined normal standards. Davies et alia (1930) again demonstrated the tendency for acidity to decrease with age, and the increase of achlorhydria which occurred in normal cases studied later in life. Harrison (1937) quotes 0.30 units as normal "free acidity" for fasting juice. MacFate (1937) gives 5-20 units for normal fasting juice. Gradwald (1938) believes that a "free" acidity normally ranges from 20-40 units in the normal healthy adult. The Royal Infirmary, Edinburgh (1939) uses 20-40 units for the normal range for free acidity. Therefore, the standard for "free" acidity based on a composite figure will be 2½-25 units as the normal limits for fasting juice. All values above this standard will indicate hyperacidity and those below will indicate hypoacidity.

Normal total acidity in the adult is the sum of the free hydrochloric acid, loosely combined hydrochloric acid, acid salts, and organic acids. MacFate (1937) gives 15-45 units as the normal limits in the adult fasting juice and the figures exceeding 50 units as hyperacidity. Harrison (1938) gives 40-60 or 70 units for the normal range for total acidity. Therefore, the standard for "Total" acidity derived /

derived from an average of the above gives the normal range as 45-73 units with a test meal, and 12-47 units for the normal "fasting" juice, but since the total acidity is generally within twenty units of the free acidity in adults forty-five units for the maximum total acidity will be taken as the standard. Therefore infants having total acidity above this figure will be considered to have hyperacidity and those below the lowest limit will be reckoned to have hypoacidity.

The gastric diathesis in the adult. It is recognised that twenty per cent of people have chronic gastric disorders, of which half are born with the hypersthenic gastric diathesis, and approximately the other half are born with a hyposthenic gastric diathesis, both of which are often familial. Complete achlorhydria is present in about 3.5 per cent of healthy children and young adults of both sexes, but it is uncertain whether this is congenital, and the result of an inborn error of secretion, (that is, a true constitutional "achylia") or some general infection in infancy or early childhood with an extreme degree of constitutional hypochlorhydria. Among healthy adults of twenty years of /

of age four per cent have achlorhydria, between 30-39 years of age eight per cent have achlorhydria, of those aged 40-49 twelve per cent have achlorhydria, but in the next three decades taken together there is only a further rise of four per cent. (Price 1937).

Having fixed these arbitrary standards the gastric analysis of sixty-four unfed mature infants and sixty-four unfed premature infants will be given.

No.	Weight. Lb.	Oz.	pH.	Gunzberg Reaction.	Free Acid. In units.	Total Acid. In units.	Sex.	Vol. of Juice.	Remarks.	Pregnancy.	Progress of Infant in Hospital
1.	5	11	8-10	Negative.	0.0	14.3	F.	0.2	Bacteria.	-	Normal.
2.	5	12	3-4	Positive.	22.86	137.1	F.	1.0	-	-	Normal.
3.	5	14	3-4	Positive.	21.4	60.7		1.0	Bacteria.	-	Normal.
4.	5	15	8-10	Negative.	0.0	21.4	M.	0.2	Bacteria.	-	Premature by dates. Had diarrhoea
5.	5	15	3-4	Positive.	51.02	119.3	F.	2.0	-	-	Normal, but premature by dates
6.	5	15	3-4	Positive.	42.86	142.87	M.	4.0	-	-	Normal.
7.	5	15	3-4	Positive.	39.3	75.0	F.	3.0	-	-	Normal.
8.	6	1	3-4	Positive.	14.3	46.4	F.	0.2	-	Toxaemia & Antip. Haem.	Normal.
9.	6	1	3-4	Positive.	32.14	85.7	M.	2.0	-	-	? Pneumonia on fourth day.
10.	6	2	3-4	Positive.	17.86	67.86	M.	2.5	-	-	Premature by dates.
11.	6	3	3-4	Positive.	28.6	92.86	F.	4.0	-	-	Normal.
12.	6	3	3-4	Positive.	8.57	71.4	M.	2.0	-	-	Premature by dates. Diarrhoea on 4th-6th day.
13.	6	3	3-4	Positive.	46.4	107.1	M.	2.0	-	-	Normal.
14✗	6	5	8-10	Negative.	0.0	53.59	M.	2.0	-	-	Died of Spina Bifida and Hydrocephalus.
15✗	6	6	8-10	Negative.	0.0	17.86	M.	1.5	Bile.	-	Normal but premature by dates.
16.	6	7	3-4	Negative.	7.1	82.1	M.	2.0	-	-	Normal.
17.	6	8	3-4	Positive.	18.0	153.6	F.	0.2	Bacteria.	-	Normal.
18.	6	8	3-4	Positive.	10.71	46.4	M.	0.2	-	-	Normal.

No.	Weight Lb.	Oz.	pH.	Gunzberg Reaction.	Free Acid, in Units.	Total Acid, in Units.	Sex.	Vol. of Juice.	Remarks.	Pregnancy.	Progress of Infant in Hospital
19.	6	8	3-4	Positive.	35.7	103.5	F.	4.5	-	-	Progress slow due to Diarrhoea
20.	6	9	3-4	Positive.	7.1	60.7	F.	0.2	-	-	Normal.
21.	6	9	8-10	Negative.	0.0	42.86	F.	2.0	Bacteria.	-	Rapid weight gain.
22.	6	11	3-4	Positive.	17.86	53.57	F.	0.2	-	-	Premature by dates. Had Diarrhoea.
23.	6	12	3-4	Positive.	30.0	64.3	M.	1.0	-	-	Slow progress due to thrush and skin infection.
24.	6	13	3-4	Positive.	21.4	39.3	M.	0.2	-	-	Normal.
25.	6	13	3-4	Positive.	67.86	103.6	F.	7.0	-	-	Premature by dates, but progress normal.
26.	6	14	3-4	Positive.	30.7	62.9	M.	8.0	-	-	Normal.
27.	6	14	3-4	Positive.	14.29	78.57	M.	6.0	-	-	Normal.
28.	7	0	3-4	Positive.	7.14	58.6	M.	0.2	-	-	Rapid weight gain.
29✕	7	0	3-4	Negative.	7.1	64.3	F.	0.5	Specimen taken on 8 D.	-	Melaena, neonatorum and haematemesis.
30.	7	0	3-4	Positive.	50.0	92.86	F.	4.0	-	Pre-eclampsia.	Normal.
31.	7	1	3-4	Positive.	5.0	50.0	M.	0.4	-	Pneumonia.	Gained weight rapidly.
32.	7	1	3-4	Positive.	25.7	67.86	F.	2.0	-	-	Normal.
33.	7	2	3-4	Positive.	46.43	142.86	M.	6.0	-	-	Normal.
34.	7	3	3-4	Positive.	60.7	89.3	F.	5.0	-	-	Normal.
35.	7	4	3-4	Positive.	23.57	82.1	M.	2.0	-	-	Normal.
36.	7	4	3-4	Positive.	53.6	78.6	F.	4.0	-	-	Normal.

No.	Weight Lb.	Weight Oz.	pH.	Gunzberg Reaction.	Free Acid. In units.	Total Acid. In units.	Sex.	Vol. of Juice.	Remarks.	Pregnancy.	Progress of Infant in Hospital.
37.	7	4	8-10	Negative.	0.0	21.4	F.	0.2	Watery	Pre-eclampsia.	Rapid weight progress.
38.	7	5	3-4	Positive.	7.1	71.43	F.	9.0	-	-	Normal.
39.	7	6	3-4	Positive.	42.9	78.57	F.	2.5	-	-	Normal.
40.	7	7	3-4	Positive.	42.86	114.3	M.	9.0	-	-	Normal.
41✕	7	8	8-10	Negative.	0.0	21.4	F.	0.2	Blood & Bacteria.	Pre-eclampsia.	Satisfactory but had pyrexia.
42✕	7	8	8-10	Negative.	-	-	F.	1.0	Bile.	-	Normal.
43.	7	8	3-4	Positive.	42.9	71.4	M.	2.0	-	-	Normal.
44.	7	8	3-4	Positive.	28.6	46.4	F.	5.0	-	-	Normal.
45✕	7	9	8-10	Negative.	0.0	17.9	M.	0.2	Blood	-	Slow progress, had slight diarrhoea.
46.	7	10	3-4	Positive.	71.4	114.3	M.	10.0	-	Heart disease.	Slow weight progress.
47.	7	12	8-10	Negative.	0.0	62.86	M.	1.5	-	-	Slow weight progress, due to diarrhoea.
48.	7	12	8-10	Negative.	0.0	17.86	F.	0.2	-	-	Unaccountable loss of weight, bu had slight vomiting 8th-12th
49.	7	13	3-4	Positive.	53.6	107.1	F.	4.5	-	-	Normal.
50.	7	14	3-4	Positive.	10.71	64.3	M.	1.0	-	-	Normal.
51.	8	0	8-10	Negative.	0.0	71.4	F.	0.1	Watery.	-	Normal.
52.	8	0	3-4	Positive.	35.7	75.0	M.	2.0	-	-	Normal.
53.	8	2	3-4	Positive.	46.4	96.4	M.	4.0	-	-	Unaccountable loss of weight, for first 4 days of life.
54.	8	5	3-4	Positive.	21.4	57.1	F.	0.2	-	-	Normal.

No.	Weight Lb.	Weight Oz.	pH.	Gunzberg Reaction.	Free Acid. In units.	Total Acid. In units.	Sex.	Vol. of Juice.	Remarks.	Pregnancy.	Progress of Infant in Hospital
55✕	7	8	8-10	Negative.	0.0	-	M.	2.0	-	Toxaemia of pregnancy.	Died from ?erythroblastosis or congenital syphilis.
56.	8	5	3-4	Positive.	19.3	42.9	F.	2.0	-	-	Normal.
57.	8	7	3-4	Positive.	21.4	78.57	F.	4.0	-	-	Slow progress due to vomiting.
58.	8	8	8-10	Negative.	0.0	21.4	M.	1.0	-	-	Normal.
59.	8	10	3-4	Positive.	39.3	85.7	F.	2.0	-	-	Normal.
60.	8	11	3-4	Positive.	50.0	85.7	M.	2.0	-	-	Slight diarrhoea with loss of weight.
61.	8	12	3-4	Positive.	17.86	50.0	M.	5.0	-	Heart disease.	Normal.
62.	9	1	3-4	Positive.	17.9	39.3	M.	2.0	-	-	Slow weight progress.
63.	9	1	3-4	Positive.	27.1	66.4	M.	2.0	-	-	Normal.
64.	9	7	3-4	Positive.	46.43	107.1	F.	5.0	-	-	Normal.

✕ Abnormal case.

1 unit = 1 c.c. N/10 HCl per 100 c.c. gastric juice.

Volume of juice in c.c.

No.	Weight Lb.	Oz.	pH.	Gunzberg Reaction.	Free Acid. In units.	Total Acid. In units.	Sex.	Vol. of Juice.	Remarks.	Pregnancy.	Progress of Infant in Hospital.
1✗	2	1	8-10	Negative.	0.0	-	F.	-	-	-	Died, no P.M.
2✗	2	6	8-10	Negative.	0.0	107.1	M.	0.2	-	-	Died from intraventricular haemorrhage.
3.	3	4	8-10	Negative.	0.0	50.0	F.	4.0	-	Pneumonia Hb. 25%.	Slow progress.
4✗	3	5	8-10	Negative.	0.0	-	M.	-	-	-	Died with cerebral symptoms. No. P.M.
5.	3	11	8-10	Negative.	0.0	23.57	M.	0.2	Cocci	Caesarian section.	Twin to No. 7. Died from gastro-enteritis.
6✗	3	13	8-10	Negative.	0.0	50.0	F.	0.2	-	-	Died from intraventricular haemorrhage,& pneumonia.
7.	4	0	3-4	Negative.	6.4	27.1	M.	0.2	Bacteria	Caesarian section.	Twin to No. 5. Progress normal.
8✗	4	2	3-4	Positive.	7.57	56.8	M.	0.2	-	-	Died from cerebral haemorrhage.
9✗	4	2	3-4	Positive.	16.4	50.0	F.	2.0	-	-	Died from cerebral haemorrhage.
10.	4	2	8-10	Negative.	0.0	-	M.	-	Bacteria	-	Twin to No. 33. Died from broncho-pneumonia.
11.	4	4	3-4	Positive.	14.28	57.1	F.	1.5	-	-	Diarrhoea and died.
12.	4	6	3-4	Positive.	35.7	73.57	M.	3.0	-	-	Twin to No. 57. Normal.
13✗	4	7	8-10	Negative.	0.0	-	F.	-	-	-	Died from asphyxia at birth.
14.	4	7	3-4	Positive.	25.0	50.7	M.	2.0	-	-	Died from broncho-pneumonia.
15.	4	7	8-10	Negative.	0.0	-	M.	-	-	-	Normal.
16.	4	8	8-10	Negative.	0.0	42.86	F.	1.0	-	-	Twin, both normal.
17✗	4	8	8-10	Negative.	0.0	52.1	F.	1.0	-	-	Died from icterus gravis. with kernicterus.
18.	4	10	3-4	Positive.	21.4	92.86	F.	4.0	-	-	Twin to No. 28. Progress normal.

No.	Weight Lb.	Oz.	pH.	Gunzberg Reaction.	Free Acid. In units.	Total Acid. In units.	Sex.	Vol. of Juice.	Remarks.	Pregnancy.	Progress of Infant in Hospital
19.	4	10	8-10	Negative.	0.0	-	F.	-	-	-	Normal.
20.	4	11	3-4	Positive.	53.0	132.5	F.	4.0	-	Chronic anaemia.	Normal.
21.	4	11	3-4	Positive.	39.3	64.3	M.	4.2	-	W.R. Positive.	Normal and W.R. negative.
22.✕	4	12	3-4	Negative.	20.0	78.7	F.	1.75	Bile	-	Rapid weight progress.
23.	4	12	8-10	Negative.	0.0	-	M.	-	-	-	Normal.
24.	4	12	8-10	Negative.	0.0	-	M.	-	Four bacilli	-	Rapid weight progress.
25.	4	12	3-4	Positive.	57.14	78.57	F.	4.0	Bacteria	Antip. haemorr.	Normal.
26.✕	4	13	8-10	Negative.	0.0	10.71	F.	0.5	Taken on 9th day.	-	Melena neonatorum.
27.✕	4	13	8-10	Negative.	0.0	60.0	M.	0.2	-	W.R. positive.	Normal, but W.R. positive.
28.	4	13	3-4	Positive.	36.0	75.0	F.	0.2	-	-	Normal.
29.	4	15	3-4	Positive.	7.1	42.86	F.	2.0	-	-	Twin to No. 18. Progress normal.
30.	4	15	8-10	Negative.	0.0	9.29	M.	2.0	Four bacilli.	-	Normal.
31.	5	0	8-10	Negative.	0.0	35.7	M.	0.3	-	Caesarian section.	One of twins - other died. Progress normal.
32.	5	0	3-4	Negative.	28.57	71.43	M.	3.0	Four organisms.	-	Normal.
33.	5	0	8-10	Negative.	0.0	60.71	F.	1.2	Few cocci.	-	Very slow progress due to diarrhoea.
34.	5	0	8-10	Negative.	0.0	-	F.	-	Bacteria.	-	Normal. Twin to No. 10.
35.	5	0	3-4	Positive.	5.71	53.57	F.	2.1	Bacteria.	Antip. Haemorr.	Slow weight progress. Twin to No. 43.
36.	5	0	8-10	Negative.	0.0	32.1	M.	2.0	-	-	Normal.

No.	Weight lb.	oz.	pH.	Gunzberg Reaction.	Free Acid. In units.	Total Acid. In units.	Sex.	Vol. of Juice.	Remarks.	Pregnancy.	Progress of Infant in hospita
37 ✕	5	1	8-10	Negative.	0.0	10.7	M.	0.2	Watery.	Pre-eclampsia.	Died from cerebral haemorrha and pneumonia.
38.	5	1	3-4	Positive.	17.86	50.0	F.	0.2	-	-	Rapid weight progress.
39.	5	1	3-4	Positive.	11.3	130.3	M.	0.2	-	-	Rapid weight progress.
40.	5.	1	3-4	Positive.	42.86	135.7	M.	5.0	-	-	Normal.
41.	5	2	3-4	Positive.	14.3	64.3	M.	0.2	-	-	Normal.
42.	5	2	3-4	Positive.	32.1	64.29	M.	0.2	-	-	Normal.
43.	5	3	3-4	Positive.	10.7	32.1	M.	0.2	-	-	Normal.
44.	5	4	3-4	Positive.	7.1	50.0	M.	0.1	-	-	Normal.
45.	5	4	3-4	Positive.	34.0	64.3	F.	5.0	-	-	Normal.
46.	5	4	8-10	Negative.	0.0	35.7	F.	0.2	Bacteria.	Antip. haemorr.	Twin to No. 34. Very slow progress.
47.	5	5	8-10	Negative.	0.0	71.4	F.	0.2	Bacteria.	-	Normal.
48.	5	5	3-4	Positive.	-	-	F.	-	-	-	Normal.
49.	5	5	8-10	Negative.	0.0	-	M.	2.0	-	-	Normal.
50.	5	5	3-4	Positive.	17.86	60.0	F.	2.0	four bacilli.	-	Normal.
51.	5	5	8-10	Negative.	0.0	14.3	F.	0.4	no mucous.	-	Normal.
52.	5	5	3-4	Positive.	35.7	85.7	F.	4.0	-	-	Normal.
53.	5	6	3-4	Negative.	3.6	46.43	F.	4.0	Bacteria.	-	Died at 3 weeks old from enteritis.
54.	5	6	8-10	Negative.	0.0	-	F.	-	-	-	Slow weight progress.

No.	Weight Lb.	Oz.	pH.	Gunzberg Reaction.	Free Acid in units.	Total Acid in units.	Sex.	Vol. of juice.	Remarks.	Pregnancy.	Progress of Infant in Hospital
55.	5	6	3-4	Positive.	30.0	113.6	M.	4.5	-	-	Normal.
56✕	5	6	8-10	Negative.	0.0	-	M.	-	Watery.	-	Died from cerebral haemorrhage and pneumonia.
57.	5	6	3-4	Negative. ?	7.1	110.0	F.	0.2	-	Heart disease.	Normal. ? 2 twins.
58✕	5	6	3-4	Positive.	12.14	44.3	F.	3.0	-	Bronchitis & pleurisy.	Died ? cerebral haemorrhage. No P.M.
59.	5	6	3-4	Positive.	28.57	60.7	F.	4.0	-	Pre-eclampsia.	Twin - other twin mature. Progress normal.
60.	5	7	3-4	Positive.	21.43	53.57	M.	0.2	Cocci	-	Normal.
61.	5	8	3-4	Positive.	53.57	82.14	M.	6.0	-	-	Twin to No. 12. Progress normal.
62.	5	8	3-4	Positive.	21.4	53.6	F.	2.0	-	Appendicitis, peritonitis.	Normal. (Caesarian section.)
63.	5	8	3-4	Positive.	39.3	75.0	M.	1.5	-	Pre-eclampsia.	Normal.
64.	5	8	8-10	Negative.	0.0	11.3	M.	0.4	-	-	Normal.

✕ Abnormal case.

1 unit = 1 c.c. N/10 HCl per 100 c.c. gastric juice.

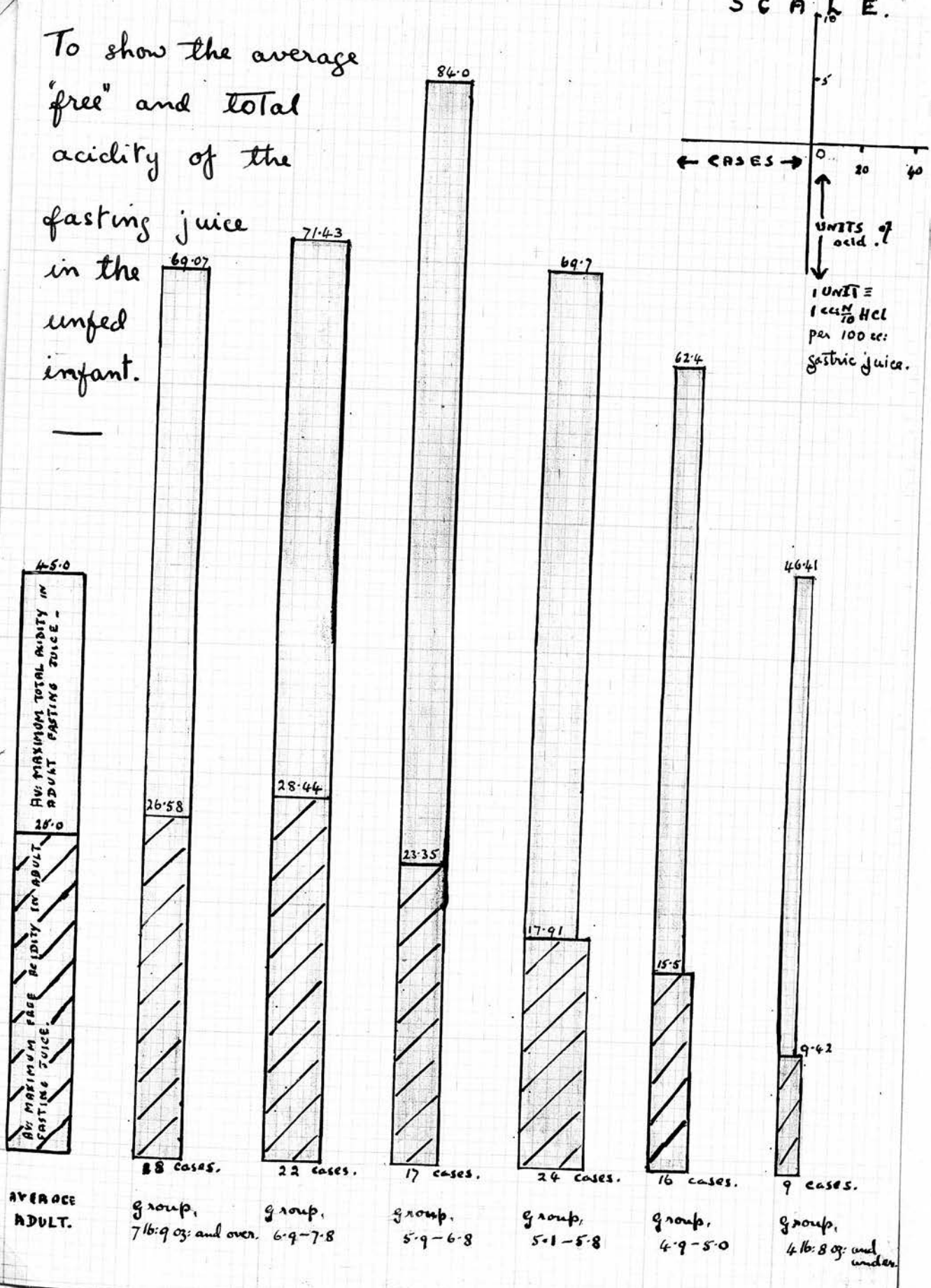
Volume of juice in c.c.

The Results on the Gastric Investigations on the Newborn Infant.

(A) 64 cases of the unfed mature infant.

(B) 64 cases of the unfed premature infant.

To show the average "free" and total acidity of the fasting juice in the unfed infant.

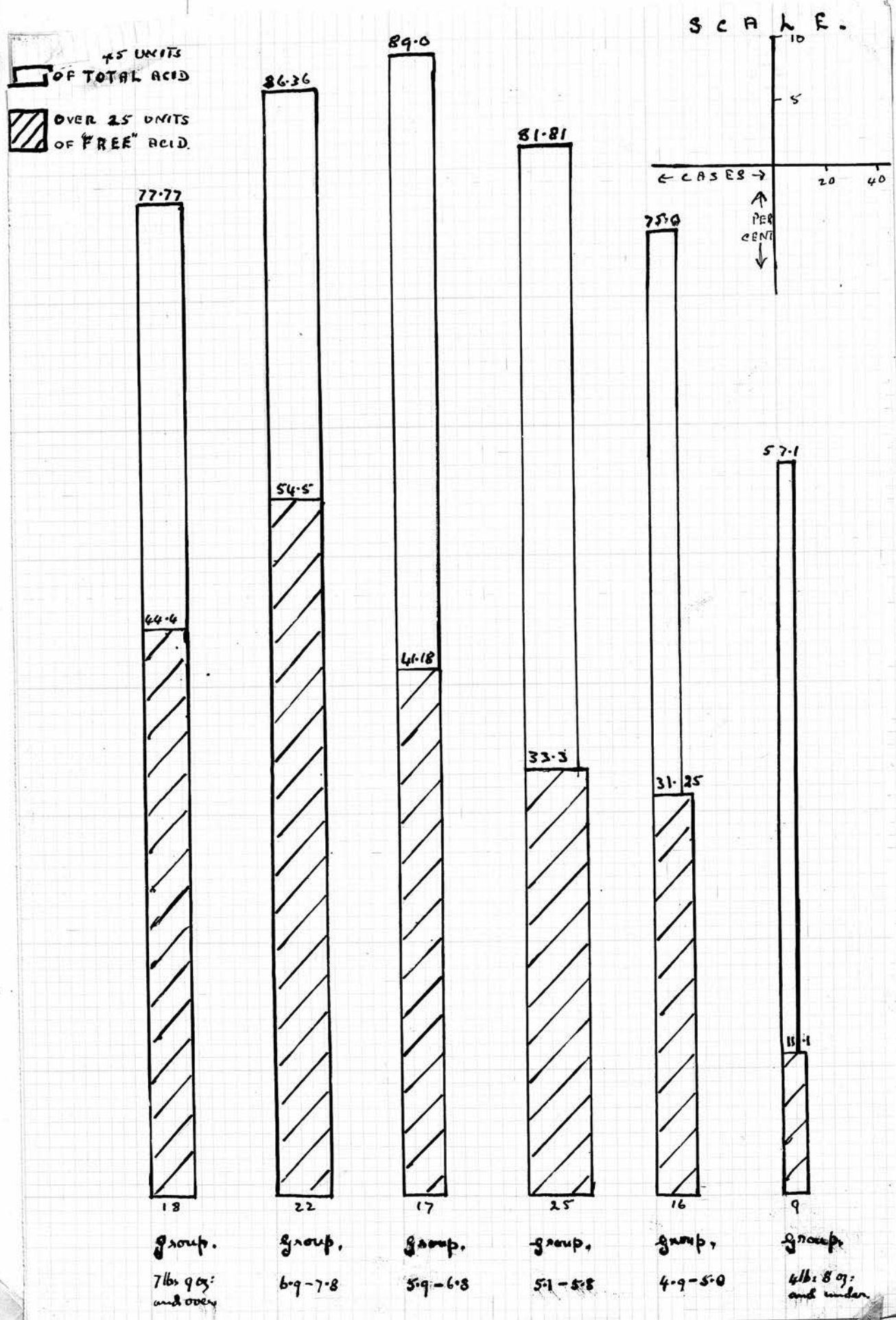


The Discussion on the Results of Gastric Investigations on the Newborn Infant.

The average free and total gastric acidity. This is expressed on the opposite page. The mature and premature infants are divided into groups in order to show that the heavier the infant is at birth the greater is its chance of having a more potent gastric secretion. All the groups, however, have a reasonable amount of "free" and total acidity, in fact the total acidity exceeds 45 units*, the arbitrary standard adopted for the indication of hyperacidity. Hyperacidity as judged by "free" acidity exceeding 25 units means that the two groups of infants above 6½ lb. can only be put into this category. Another interesting observation is that the relationship between the quantities of free and total acidity is different to that in adults. In the infants investigated there is a difference of 40-50 units between the two estimations, whereas in adults there is generally a maximum difference of 20 units. To compare the results with those of children aged 4-12 yrs. who have on the average 15 units free acidity and 32 units total acidity /

* I units = Icc: $\frac{N}{10}$ HCl per 100cc: gastric juice.

acidity in their fasting juice, (MacFate 1937), it is evident that the newborn have a more concentrated secretion. It can be shown that infants of a year old have a "free" acidity of 6 units and a total acidity of 3-12 units after a test meal, or that infants under a year old frequently have no free acid after a test meal,(MacFate 1937) but the results cannot be compared with the acidity of the fasting juice of the newborn. In the past this mistake has probably been made as it has been the general belief that the gastric secretion becomes more copious and concentrated with increasing age. From the investigations on the newborn it must be concluded that the gastric secretion is extremely concentrated in the newborn, although it is very scanty. If this view is adopted it will explain the frequency with which achlorhydria is present in infants under one year old after they are given a test meal, and the reason for low values for gastric acidity in childhood. Although the secretion becomes less concentrated with age as supported by MacFate's figures already quoted, the author has shown that children of 4-12 years of age are capable of secreting a more concentrated /

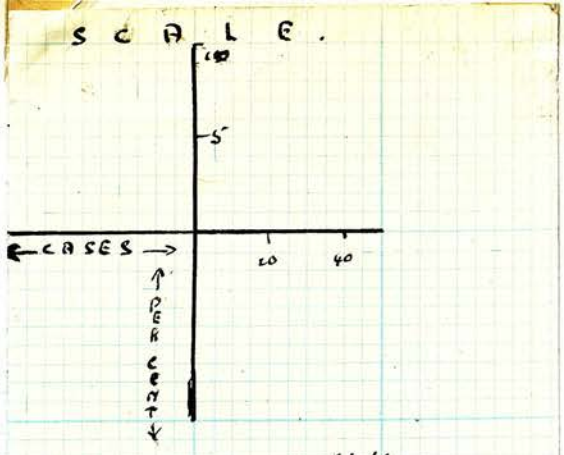

45 UNITS OF TOTAL ACID
OVER 25 UNITS OF "FREE" ACID.
SCALE.
10
5
← CASES →
20
40
PER CENT
77·77
44·4
18
Group.
7lbs 9oz: and over
86·36
54·5
22
Group.
6·9 – 7·8
89·0
41·18
17
Group.
5·9 – 6·8
81·81
33·3
25
Group.
5·1 – 5·8
75·0
31·25
16
Group.
4·9 – 5·0
57·1
11·1
9
Group.
4lbs 8oz: and under

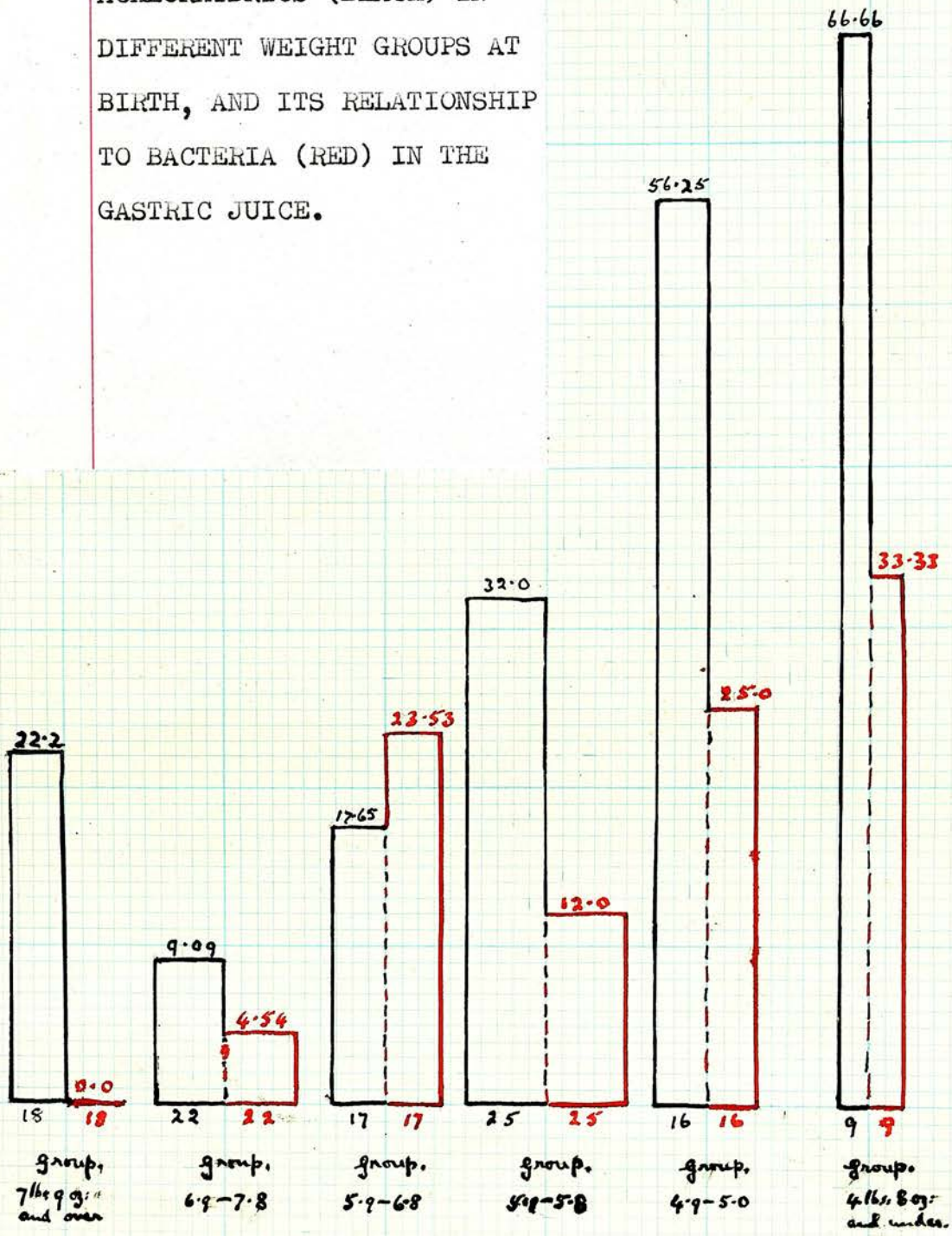
concentrated juice than adults. The average maximum free acidity after a histamine injection in these children being 92 units* and total acidity 108 units, while the average adult will have a maximum free acidity of only 70-80 units and a total acidity of 80-100 units.

Hyperchlorhydria in the newborn. The standards fixed arbitrarily are acidity above 25 units of free acid or a total acidity of over 45 units. The percentage of infants showing the condition are represented diagramatically on the opposite page. The conclusions that may be drawn from this study are that the heavier the infant is at birth the greater is the chance of hyperacidity occurring, and that the condition occurs far more frequently than used to be thought. With the above theory that the gastric juice is abnormally concentrated the results are not surprising. If hyperacidity is judged by the amount of total acid in the fasting juice the number of infants with hyperchlorhydria is about forty per cent greater. The clinical significance of the findings is not important, for there is a relative hypo-secretion in the newborn. Neither is there any relation /

* Neale et alia (1931) quotes 110 units for "free" acidity in young children after the histamine test.

TO SHOW THE PERCENTAGE OF ACHLORHYDRICS (BLACK) IN DIFFERENT WEIGHT GROUPS AT BIRTH, AND ITS RELATIONSHIP TO BACTERIA (RED) IN THE GASTRIC JUICE.





relation to the percentage of individuals with hyperacidity in adult life.

Hypochlorhydria in the newborn. Hypoacidity exists in infancy but, for simplicity, the discussion will be confined to those with achlorhydria. The graph on the opposite page gives the percentages of infants with achlorhydria. From it it can be seen that achlorhydria rapidly increases with the degree of prematurity of the infant. Prematurity as a cause of hypoacidity should be emphasised rather than the weight of the infant. e.g. It will be noticed that all infants of 5½ lbs. or under, are premature and that six mature infants were premature according to weeks gestation. Of these infants two had achlorhydria, but in one case it was probably due to the bile which was present, while four out of the six had a hypochlorhydria, and of these three had diarrhoea. The general health of the infant may also be responsible for achlorhydria. This is seen from the following table which includes twenty-one abnormal juices or juices from abnormal infants.

	Cases.	Achlorhydria.	Percentage.
Normal mature infants.	57	4 M, 5 F	15.78
Abnormal mature infant.	7	7	100.00
Normal premature "	50	12 M, 11 F	46.00
Abnormal Premature "	14	10	71.43
Total	128	49	38.28

The /

The prognosis of those which have apparently no pathological process present is, on the whole, favourable, in fact some gain weight extremely rapidly while others contract diarrhoea or progress very slowly. When achlorhydria was associated with disease at birth the infant always died.

The treatment of achlorhydria is to give a digestible acidified feed to aid digestion and prevent bacterial proliferation in the stomach and intestinal tract. The latter is important as the bacteria aggravate intestinal dyspepsia and, moreover, the premature infant which is unable to withstand infection has been shown to have a corresponding increase in gastric organisms along with the increase in achlorhydria. (See page42) In the adult bacteria are normally present in the gastric juice; they may amount to 100,000 organisms per c.c. chiefly consisting of B. Coli, staphylococci and non-haemolytic streptococci. (Wright 1937). On the other hand MacFate (1937) merely says they are never numerous /

numerous except in cases of achlorhydria when the bacterial flora is great. He also adds that the bacteria as a rule are of little or no interest with regard to the aetiology of disease, presumably because the bactericidal power of gastric juice probably prevents virulent organisms from entering the duodenum alive, but when achlorhydria is present the bacteria flourish and pass down the normally sterile duodenum to invade the small intestine. In addition, owing to the increased alkalinity of the intestinal contents the bacteria from the colon ascend into the small intestine. This predisposes to intestinal upsets and to allergic conditions, e.g. asthma, urticaria and skin diseases. Therefore the presence of numerous bacteria in the stomach contents of the premature infant, or even any infant must be an important factor in influencing their health and prognosis. This is illustrated by mature infant No. 5 and No. 41, also by premature infant Nos. 5, 7, 34, 43 and 49. It is on this account that lactic acid feeds for this type of infant should be advocated.

The Gunzberg Reaction in the newborn. This reaction is specific for hydrochloric acid and the results /

results are given in the following table:-

Cases.	% Negative Gunzberg R.	%pH 8-10	% Cases Achlorhydria.
57 mature	15.78	14.03	15.78
50 premature	46.0	38.0	46.0

The per centage of the mature infants with a negative Gunzberg Reaction is identical to the figure quoted by Tomotake (1930) who based his figure on tests carried out on fifty-two newborn infants and thirty-five older infants. Other authors, such as Hess, Tange and Pollitzer believed that "free" hydrochloric acid was always present in the gastric contents of the newborn. The difference in opinion may be partly explained by the fact that the latter authors diagnosed the presence of hydrochloric acid by estimating the pH of the gastric contents with congo red and phenophthalein.

The Influence of Abnormal or Normal Constituents in the Gastric Juice. They are:-

(A) Blood. This was present in two mature infants which were not included in the series of normal cases. The source of the blood was probably the result of the infant swallowing it at birth.

(B) Bile. It was present in one premature infant /

infant and two mature infants at birth. They were similarly discounted. The presence of bile is due to duodenal regurgitation which takes place in normal individuals, (Stewart and Dunlop 1937) and it depends on the behaviour of the pyloric sphincter. (Wright 1937).

(C) Mucus. In adults the mucus present in the stomach varies with the acidity of its contents. In the people with hyperacidity mucus is absent, while in those with achlorhydria mucus is copious. In the newborn this is not true, for mucus was present in approximately 90% of the cases. The proportion of mucus was generally greater in the juice with a low acidity, but even with hyperacidity the juice in most cases could not be separated from the mucus. Thus, in many cases when 0.2 c.c. was pipetted for titration considerable suction was necessary, and to discharge the amount from the pipette force was needed. Owing to the marked viscosity of the juice there was difficulty in withdrawing the entire quantity of resting juice. The small catheter frequently became blocked and sometimes a larger catheter had to be used. It is on this account that the results can only be said to give the impression /

impression that the resting juice increases with the acidity of the juice. The reason for the abundant mucus secretion is explained by the histological investigations on the stomach. It has been observed that in the foetal stomach the mucus secreting cells are the first to appear and they give rise to the more specialised oxyntic and peptic cells. At birth the mucus secreting cells predominate, and the number of more specialised cells are relatively less than in the adults.

(D) Liquor Amnii. After examining the hundred and twenty-eight gastric juices there was not one which contained liquor amnii, but about 75% of the specimens contained nucleated squamous cells, and a few also had some cells of the gastric mucous membrane. The absence of the amniotic cells can only be accounted for by the motility of the stomach.

The health in pregnancy. This affects the foetus or infant under certain circumstances. It is difficult to assess the injurious effects as the impairment of the mother's health may be during the pregnancy or at the time of parturition. Again, it may be mild or severe, acute or chronic, but we may assume that when the health of the infant is involved the /

the gastric secreting power will almost always be simultaneously affected. This can be accounted for by the placental barrier to infection breaking down and allowing a generalised systemic disturbance to occur in the infant. Such a failure on the part of the placenta is a rare one, only occurring when the mother has a very severe toxaemia. (Curtis 1933). Even with such toxaemia sufficient to kill the child the liver is rarely damaged, thus proving that the placenta probably maintains part of its protective function even after the death of the foetus.

(A) Severe pre-eclamptic toxaemia. 50 per cent of the infants die, either in utero or from premature birth due to spontaneous or therapeutic induction of labour, or from the toxaemic condition. (Johnstone 1937 and Beck 1937). With eclampsia the prognosis for the foetus is similar. (Johnstone 1937).

(B) Nephritic Toxaemia results in about 50 per cent mortality. (Johnstone 1937).

(C) Deficiency Diseases of the mother, such as calcium, phosphorus and vitamin D. If the deficiency is severe, the foetus will show radiological evidence of rickets. Vitamin E deficiency in the mother is supposed to be the cause of premature births in some instances, /

instances, and experimentally it has resulted in cretinism in young rats. (Young 1939).

To study the effect of the maternal health upon the foetus in the series of cases being investigated a table has been specially constructed.

Acute maternal conditions.	Effect upon the Infant.	Infant's progress.
2 penumonia	1 mature. 1 premature, had achlorhydria.	Normal, but premature slow.
1 bronchitis & pleurisy.	Premature.	Died, cerebral haemorrhage.
3 Antepartum haemorrhage.	All premature. 1 achlorhydric.	2 very slow, others normal.
1 appendicitis & peritonitis.	Premature. Delivered by Caesarian section.	Normal.

Chronic maternal conditions.	Effect upon the Infant.	Infant's progress.
1 anaemia	Premature.	Normal.
2 syphilitic	Both premature, 1 achlorhydric.	Normal.
6 pre-eclampsia	4 mature. 2 premature, 3 were achlorhydrics.	1 died, rest normal.
3 cardiac disease. (Compensated).	2 mature, 1 premature.	1 slow, others normal.

In reviewing the health of the infants belonging to these nineteen mothers, twelve progressed normally and /

and the rest showed a retarded rate of growth. This abnormality was terminated by death in two instances. These facts indicate that ill health increases in infants when they are born of mothers who are not bodily fit, particularly if they are acutely ill. Moreover, acute diseases in the mother as compared with chronic is responsible for a greater number of premature births which, in its turn, reduces the chances of survival on the part of the infant.

Sex in the newborn. Its influence upon the gastric acidity has been recorded by Tomotake (1930) who stated that male infants had a greater acidity than females. In adults this is definitely true, the former usually secreting about ten units more than the latter, provided comparable ages are tested. Figures taken from the present series of normal newborn infants contradict this view.

	Mature Infants.		Premature Infants.	
	Cases.	Units of acid per case.	Cases.	Units of acid per case.
Free Acid				
Male.	28	24.0	24	14.78
Female.	28	27.6	25	14.92
Total Acid				
Male.	28	66.66	24	57.09
Female.	28	75.57	25	62.84

In /

	No.	Cause of death.	Remarks.
Mature Infants.	55.	? Erythroblastosis or Congenital syphilis.	Achlorhydria.
	14.	Hydrocephalus.	Achlorhydria.
Premature Infants.	1.	? Prematurity, no P.M.	Achlorhydria.
	2.	Cerebral haemorrhage.	Achlorhydria.
	4.	? Cerebral haemorrhage, No P.M.	Achlorhydria.
	6.	Cerebral haemorrhage.	Achlorhydria.
	8.	Cerebral haemorrhage.	7.56 units free acid.
	13.	Asphyxia.	Achlorhydria.
	17.	Icterus gravis with kernicterus.	Achlorhydria.
	37.	Cerebral haemorrhage.	Achlorhydria.
	57.	Cerebral haemorrhage, and pneumonia.	Achlorhydria.
	59.	? Cerebral haemorrhage, No P.M.	12.14 units free acid.
	9.	Cerebral haemorrhage.	16.4 units free acid.

In concluding, female infants at birth have on the average 0.1-3.6 units "free" acid more than male infants in their fasting juice, and 5.8-9.0 units total acid more than the male.

The Health of the Infant. It is well known that the health of the infant influences gastric secretion, therefore, those infants with congenital deformities and cerebral injuries, or those which were still-born could not be considered normal. On reviewing the twenty-one cases which were rejected from the normal series it is seen that thirteen of them died and that they all had hypoacidity. (See opposite.)

The consistency with which achlorhydria or hypoacidity is present is astonishing. One would think that there was some connection between achlorhydria and cerebral haemorrhage. Experimentally it has been shown that lesions in the hypothalamus disturb gastric secretions and that gastric ulcers may develop in these cases. Therefore, it is more probable that the cerebral injury is primary to the achlorhydria. In the case with asphyxia the pH of the blood is bound to be affected and the chance of the gastric acidity being upset is great. Achlorhydria in the remaining /

remaining two cases, erythroblastosis and icterus gravis, may be primary or secondary to the disease. If it were primary it would be likely that there would be histological changes in the stomach mucous membrane, which were not observed in the one case of erythroblastosis that was examined. Again a primary lesion in the stomach is unlikely, as there is no evidence that the intrinsic factor in the stomach necessary for haemopoesis is missing. Therefore, achlorhydria is probably secondary to the infant's disease.

Practical Applications of the Results Obtained from the Gastric Investigations.

Acidifications of artificial milk feeds. The acidification of milk feeds for ill or under-nourished infants is rational and to be advocated, but the routine use of this type of food in the mature infant is unnecessary. In the premature infant particularly of 4½ lbs. and under, artificial or supplementary feeds would be advisable for the first few weeks of life. Waddell et alia (1937) suggest this after their many years of clinical experience.

Congenital /

Congenital Achlorhydria. Whether this condition exists or not, is a matter of dispute. It is for this reason that the achlorhydrics discovered in this series of cases would be worth investigating at a later date in life. If this were done a histaminic test would be preferable, and it would be necessary to have it done when the child was in good health. The explanation of hypochlorhydria or achlorhydria is not known, but the two theories are given by Wright (1937).

1. In some cases it is due to the action of mucus, saliva and bile. In fact, one group of workers have concluded that the curve of acidity is regulated mainly by the degree of regurgitation of alkaline fluid from the duodenum which, in its turn, depends on the behaviour of the pyloric sphincter.

2. An alternative interpretation of the acidity curves, which is receiving increasing support, is that the neutralisation is mainly affected by an alkaline fluid which is secreted by the pyloric region of the stomach and not by the regurgitation of the duodenal contents.

The Aetiology of Peptic Ulcers. In the past peptic /

peptic ulcers in the newborn or in infancy, or even in childhood were thought to be the result of a thrombosis of one of the small vessels in the duodenum or, less frequently, in the stomach, followed by digestion of the affected area. Considerable evidence was in favour of the infection theory as the primary cause of the thrombosis because of the association of burns with ulcers. The predisposing causes were thought to be the lowering of the vitality of the infant and previous digestive disturbances. (Paterson, 1922). More recent literature on the aetiology of ulcers can only be obtained from work done on the adult. Wyllie (1938) gives a review on the causation and treatment of peptic ulcers in the adults, and states that "whether the neurogenic theory or some other is the primary aetiological factor, the most important single factor predisposing to its production and its persistence would appear from recent research to be an abnormally high concentration of free hydrochloric acid in the stomach." Thus, after carrying out the gastric investigations on the newborn there is no reason why the same aetiological and predisposing factors for ulcers in children and infants should not be identical to those in adults. /

adults. The reason for their rarity in infancy and childhood is that at this age there is gastric hyposecretion, and the excessive mucus production acts as a protective covering to the stomach. Thus, the highly concentrated acid secretion is prevented from acting on the mucous membrane of the stomach.

Diagnosis of haemorrhagic disease in the newborn. This is sometimes extremely difficult, for, clinically, melæna is the commonest sign of the disease (Parsons and Barling 1933) and if it occurs without any other manifestation it is impossible to differentiate the condition from peptic ulcer with melæna. With the latter disease melæna is present in fifty per cent of cases. (Paterson 1922). At autopsy the two conditions may show gastric or duodenal ulceration. (Parsons and Barling 1933). Provided that hyper-acidity is a factor in the production and persistence of peptic ulcers, it is suggested that gastric analysis should be used for the diagnosis of peptic ulcer and haemorrhagic disease of the newborn. With this object in view two cases of supposed haemorrhagic disease of the newborn were examined. A mature infant, No. 29, had a history of melæna during the second /

second and fifth day of life. It also vomited blood on the second and third day of life but, apart from these symptoms, the infant made a speedy recovery after intramuscular injections of blood. Its gastric acidity was estimated on the fasting juice on the eighth day of life. It had a "free" acid of 7.1 units, and a total acidity of 64.3 units. The test when repeated on the eleventh day showed that there was no "free" acid and the total acid was 42.86 units. On neither occasion was there any hydrochloric acid present. The second case of haemorrhagic disease was a premature infant, No. 26, which had a history of melaena on the second day of life. After blood injections the infant progressed normally. Its fasting juice was taken on the ninth day of life and it contained no hydrochloric acid or free acid and the total acidity was 10.71 units. Therefore, in both cases the diagnosis of haemorrhagic disease of the newborn is supported by the investigations. The results of a larger series of such cases would be interesting.

Intestinal Disorders. The younger an infant is the greater is its predisposition to intestinal upsets. /

upsets. Over feeding is also apt to precipitate intestinal disturbances. This is possibly due to the long periods of low acidity of the stomach contents, partly because of the feeble gastric secretion and partly on account of the excessively large quantities of food which neutralises the acid. The treatment of such cases is to correct the diet and, if need be, to acidify the feeds.

CHAPTER IV.

THE HISTOLOGY OF THE STOMACH.

The introduction of histology of the stomach is to attempt to substantiate and explain the sub-normal gastric secretion in infancy and, particularly, in the premature infant. For this purpose it has been necessary to collect a series of cases because, in the past, histological work has been confined in the human being to the adult. References to standard works in histology by Schafer (1938) and Maximow (1938) were used when studying the stomach of infants and adults. The normal structure of the stomach will be described under four headings. The first three will only be briefly mentioned as they are not concerned with gastric secretion.

1. The serous or outer coat is derived from peritoneum and is, therefore, deficient on the lesser curvature.

2. The muscle coat consists of three layers of plain muscle fibres arranged in bundles. The outer ones run circularly, while those of the inner layer run obliquely. The longitudinal and circular bundles become thicker and stronger towards the pylorus and at /

at the pylorus itself the circular layer is greatly thickened to form the sphincter muscle.

3. Submucous coat is a layer of areolar tissue serving to unite the mucous membrane loosely to the muscle coat.

4. Mucous Membrane. In the very young embryo the stomach is lined by an even layer of pseudo-stratified columnar epithelium. Later, small pits begin to project into the mesenchyme. At the foot of these cavities solid buds of granular cells appear which in turn give rise to the future "parietal" and "zymogenic" cells of the gastric glands. (Maximow 1938). Lim (1932) also adopts this view but expresses it by saying that the mucus secreting cells give rise to the more highly specialised secreting cells. At birth the mucous membrane is a soft thick layer whose inner surface is covered with columnar epithelium which secretes mucus. If mucus production is very active the outer poles of the cells may be cast off with the secretory product. The columnar cells on the surface are prolonged into the ducts of the glands, but when these divide to form tubules the cells become shorter and lose their mucus secreting character. However, an occasional columnar cell may /

may be seen in the tubules and, on the other hand, both oxyntic and central cells may be seen in between the columnar cells of the ducts. At birth the length of the glands equals only half the thickness of the mucosa, but as times goes on the number of the glands gradually increases, partly through the division of the blind ends of the tubules and, partly, through the formation of new buds of undifferentiated cells. (Maximow 1938). Where the oesophagus passes into the stomach the stratified epithelium lining the gullet gives place abruptly to the columnar epithelium of the stomach. Between the glands there is reticular tissue in the meshes of which are many basophil connective tissue cells and leucocytes. The following varieties of gastric glands are :-

Glands of the cardia. These are comparatively few in number. They are usually found close to the oesophageal opening and are of two kinds - (a) simple tubules, and (b) small tubulo-racemose glands. The secreting tubules of the racemose glands are lined by cells which are granular in appearance and of a short columnar form.

Glands of the fundus. In these glands the tubules /

tubules are usually long and the duct short. The epithelium of the tubules is mainly composed of two kinds of cells, termed from there relative position in the tubules:- (1) The Central. (2) The Parietal.

The central cells have a spherical nucleus generally near the middle of the cell and the cytoplasm of the cell is granular. Such cells are called "peptic" cells. In addition to these there occurs another type of central cell which is larger and clearer, having no obvious cytoplasmic granules. The cell nucleus is flattened or wedge-shaped. Such a cell is named a "mucoid" cell.

The parietal cells are scattered along the tubule lying between the central cells and the basement membrane. They are ovoidal or spheroidal in shape and each contains a round nucleus near its centre. These are parietal or "oxyntic" cells, and are believed to be concerned with the production of hydrochloric acid of the gastric secretion. In the adult these cells may be also found in the neck of the gland, or even on its surface. In fact Cowdry (1932) and Maximow (1938) state that in the adult they are more numerous in the neck of the gland.

The /

The former also says that the granular appearance of the cells is due to the presence of numerous small granules of low refractive power situated in the cytoplasm.

Glands of the body. These glands show the transition of the fundal type of structure to that of the pylorus in that the ducts are short at the cardiac end and long towards the pylorus. The ducts are lined with columnar cells and the glands with mucous secreting, oxyntic, and central cells in varying proportions.

Glands of the Pylorus. The ducts are very long passing into the submucous layer, and the secreting tubules possess cells of only one kind. These appear to correspond with the mucoid cells of the fundal gland, that is, the nucleus is flattened and situated at the base of the cell and the cytoplasm is granular in appearance. They are said to yield pepsin but are different from the peptic cells of the fundus..

The Histology of the Stomach of the Newborn Infant.

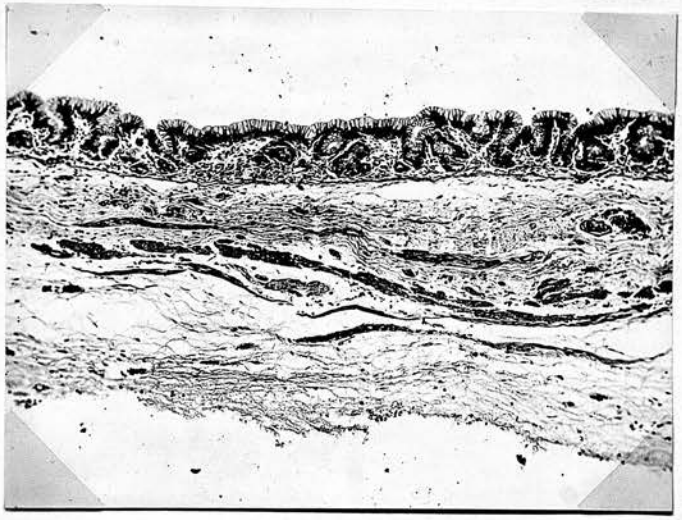
Owing to the lack of knowledge and the absence of /

of literature on the histological appearance of the mature and premature infant's stomach a series of cases has been studied. For comparison with the adult stomach two cases were obtained and, microscopically, they closely resemble the illustrations given by Maximow (1938) and Bremmer (1927).

The technique of obtaining the specimens from the newborn infant was to run or force 10 per cent formol saline into the stomach immediately after death. Later, at the post-mortem, portions of the stomach were taken from the cardio-oesophageal junction, fundus, body and pylorus. To obtain the adult specimen it was necessary to wait for a surgical operation for gastrectomy and the removed tissue was immediately placed in the fixative. After all the specimens had been fixed they were sectioned in the usual way and stained with haematoxylin and eosin. Additional sections of the fundus and the body were stained with eosin and methylene blue in order to show the oxyntic cells more vividly as a bright pinkish red cell. The only difficulty that arose was in the preserving of the specimens within half an hour of death. If the precaution is not taken an accurate microscopical study /

study is impossible because autolysis rapidly destroys the normal structure of the mucous membrane. (Hadfield and Garrod 1938).

SECTIONS OF FUNDUS OF STOMACH.



Case No. 1. Magnification x 70.
To show primitive development of stomach.

Case No. 8. Magnification x 70.
To show well developed stomach of mature infant.

Reports on the Histological Examinations made on stomachs of Newborn Infants.

Case 1. Weight 2 lbs. 6 ozs. Male. Died within a few hours of birth from intraventricular and sub-dural haemorrhage. Its gastric juice at birth contained no hydrochloric acid. At post mortem the stomach was distended with formalin solution and this resulted in the folds of the mucous membrane being absent in the histological examination. The mucous membrane was half the thickness of that found in mature infants. The glands were very primitive in character, being shallow and seldom branched. They were reduced in number as evidenced by the fact that portions of the membrane contained no ducts. The four sections from the stomach all had this primitive appearance. The sections from the fundus and the body showed very few oxyntic cells which were situated in the fundus of the primitive gland.

Case 2. Weight 2 lbs. 14 ozs. Male. Died when two days old from intraventricular haemorrhage and extreme prematurity. The mucous membrane was grossly under developed as compared with the stomachs of mature infants. In the fundus and body oxyntic cells were seen, but they were localised to the base of /

of the primitive glands.

Case 3. Weight 4 lbs. Male. Lived only two hours. Died of bilateral subarachnoid and intraventricular haemorrhages. The left lung was largely atelectatic. The mucous membrane of the stomach was poorly developed, but the glands were longer and branched more freely than in the infants weighing under three pounds. The sections of fundus and body showed numerous oxyntic cells at the bases of the glands, but owing to their not extending towards the surface of the gland there were relatively fewer oxyntic cells than in the stomach of a mature infant.

Case 4. Weight 4 lbs. 7 ozs. Aged ½ hour. Died of asphyxia. The stomach was distended at post mortem with the formalin solution, thus the folds in the mucous membrane were obliterated. The membrane, however, was fairly well developed and approximated that of a mature infant. The glands of the fundus and the body contained a fair number of oxyntic cells which were not localised to the fundus of the glands. A few extended up into the body of the gland, but none were seen in the neck of the gland.

Case 5. Weight 4 lbs. 12 ozs. Died when eight days old from pneumonia. The mucous membrane of the /

the stomach simulated that of a mature infant by the number of glands present, their size and degree of branching. The oxyntic cells, however, were not so numerous as in infants over 5½ lbs. Moreover, they were localised to the lower half of the glands.

Case 6. Weight 5 lbs. 8 ozs. Female. Aged 2-3 hrs. Died from intraventricular haemorrhage. The stomach mucous membrane appeared to be very primitive in structure and development, resembling the membrane in infants 2 lbs. 6-14 ozs. in weight. There was a corresponding diminution of oxyntic cells which were localised to the bases of the glands.

Case 7. Weight 5 lbs. 10½ ozs. Male. Aged 8 days. Died from pneumonia and slight subdural haemorrhage. The mucous membrane was very well developed. It was thick and was crowded with racemose glands. In the fundus and body of the stomach the oxyntic cells were very numerous at the bases of the glands, and only a few extended into the body of the glands.

Case 8. Weight 6 lbs. 5½ ozs. Male. Aged 24 hours. Died from meningocele and internal hydrocephalus. The stomach membrane was thick and packed with racemose glands. The oxyntic cells were numerous and a few /

few were seen just below the neck of the gland. As usual these cells were chiefly lying at the base of the glands.

Case 9. Weight 7 lbs. 4 ozs. It was 8 days old when it died from pneumonia. On examination of the stomach it was noted that it had probably the thickest membrane of all the specimens. The oxyntic cells were also exceptionally plentiful, but the bulk of them were to be found at the fundus of the glands. A few were seen fairly close to the surface but did not lie in the neck of the gland.

Case 10. Weight 7 lbs. 8 ozs. Male. Died within a few hours of birth from ? erythroblastosis or congenital syphilis. The stomach was one of the best developed of this series. The oxyntic cells were seen close to the surface of the mucous membrane but, as in all the other cases, the majority of these cells were at the bases of the glands.

Cases 11 & 12. These stomachs were both obtained from adults. They had the normal structure as described in text-books on histology. The most striking difference in contrast to the infant's stomach was that the oxyntic cells were fairly uniformly distributed throughout the body and neck of the glands, /

glands, but were definitely not more concentrated at the bases of the glands.

In summarising the sequence of development of the gastric glands it can be said that the three cases weighing less than 4 lbs 7 ozs. had a very primitive structure. When infants attained this weight the gastric glands became fairly well developed except for the number of oxyntic cells present. These cells became most numerous in infants weighing 6 lbs. 5½ ozs. or more. In comparison with the adult stomach the infant's mucous membrane was relatively thinner but was equally well developed. The oxyntic cells, however, were in proportion probably less than in the adult. Lastly, the only case which did not fit into the series of cases to show the gradual glandular development with the increase of body weight was No. 6 which weighed 5½ lbs. and had an abnormally primitive mucous membrane. Unfortunately, no explanation can be offered except that it be due to retardation in development or a congenital deficiency. The results are of value in that they explain or support the following observations:-

1. By the weight progress charts of the newborn infant it was noted that those weighing 4½ lbs. or less /

less, gained weight exceptionally slowly. This fits in with the observation that the same group of cases has a gastric mucosa of a generalised primitive structure.

2. The gradual diminution of "free" acidity in the infants under 6½ lbs. can be accounted for by the progressively diminishing number of oxyntic cells in the stomach of infants below that weight.

3. Case No. 6, which has a stomach abnormally poorly developed for its body weight, could explain the reason for achlorhydria being present in a proportion of the newborn infants. It could also throw light on the cause for certain apparently healthy infants not thriving as well as the average child of its own weight group.

CHAPTER V.

THE EFFECT OF THE DIGESTION ON THE GROWTH OF THE INFANT.

The best guide as to the progress of an infant is by its weight. Therefore, graphs of the premature infant's weight progress during the first three months of life will be studied and compared with those of mature infants. Firstly, the literature on the subject will be reviewed under three headings. Then statistics of weight progress in infancy collected at the Royal Maternity Hospital, Edinburgh, will be given and discussed.

1. The Physiological loss of Weight at Birth.

The initial loss of weight during the first few days of life is so constant that Hess (1923) considered moderate losses "physiological." The loss varied with maturity. In the mature the maximum loss on the average was 7.8 per cent of the body weight. (Pfaundler 1916). In infants of multiparous mothers it was 7.5 per cent, and in infants of primiparous mothers it was 9.3 per cent. (Pies 1911). The latter figures were confirmed by Gundobin (1912), who attributed the fact to better nursing conditions, milk /

milk appearing sooner in multiparae, and being more abundant. In the premature infant the loss was thought to be relatively greater. (Hess 1923). He gave the following examples of weight loss in the premature infant:-

Weight of Infant.	Average loss of Weight.	Per cent. of Body Weight.
800-1200 Gm.	71 Gm.	7.1
1200-1500 Gm.	97 Gm.	7.2
1500-2000 Gm.	137 Gm.	7.8
2000-3500 Gm.	177 Gm.	6.4

De Lee (1915) supported his view and adds that the nearer the infant is to full term the lower is its relative loss. This is also suggestive of figures quoted by Hess. The percentages, however, do not equal those given for mature infants. The day of maximum loss is given as the third day of life, - Ramsey and Alley (1918) who reviewed 1000 cases, but Cleland (1938) gave the fourth as the average day, and Gundobin (1912) the fourth to sixth day. Lastly Pfaundler (1916), after observing 1000 newborn infants, came to the conclusion that 42 per cent showed their maximum loss on the fourth day. The loss /

loss of weight is accounted for by:-

1. Meconium. This loss is approximately 2½ Ozs., by Camerer (1900), but Hirsch (1910) put it at 5-6½ ozs.

2. Urine. The amount voided before the child receives much fluid is probably very little.

3. Water lost via the lungs and skin.

4. The stump of the umbilical cord.

5. Loss of body tissue, of the fat, glycogen and albumin as evidenced by the loose and wrinkled condition of the infant's skin and lost turgor of the tissues generally.

6. Vomiting. This occurs in some cases during the first twenty-four hours when the stomach contents, such as swallowed liquor amnii, are lost.

The treatment or prevention of loss of weight has been demonstrated by Shick (1916). He believed the loss was avoidable, and to prove it he fed twelve newly born infants on breast milk. They were given 10 per cent of their body weight of milk in the first twenty-four hours, and then increased the amount until 15 per cent was given at the end of the third twenty-four hours. Another, but less successful /

successful, method was that of Halpern (1934) who adopted the idea from Kugelmass. An isotonic solution of 6 per cent gelatine, 3 per cent dextrose, and 0.5 per cent sodium chloride was fed to 75 newborn infants two hourly. A similar number of newborn infants fed by the orthodox methods by bottle or at the breast or with both at 3-4 hour intervals served as controls. The infants who received the hydrating solution showed an initial loss of weight of 1.4 per cent less than the controls, and regained their birth weight from 1.3 to 1.5 days sooner than the controls.

The benefit of the preventive treatment is doubtful, but such feeds would be of value in checking abnormally large falls in weight, thus preventing dehydration fever or other harmful consequences.

II. Date of Regaining of Birth Weight.

The views held by authors on this subject are somewhat varied. Gundobin (1912) quoted 11-12 days, while Pritchard (1938) allowed 7-10 days for the initial loss to be made good in the normal child. Ramsay and Alley (1918) said that only one quarter of all infants regain their body weight by the tenth day. The premature infant, however, may not regain its /

its birth weight for 20-30 days (Gundobin 1912) or for 14-21 days (Saxl 1937). Authors do agree that the breast fed infant regains its birth weight sooner than those which are artificially fed.

III. The Progressive Gain in Weight.

The standard adopted for the mature infant is the one that is in present use in the Royal Maternity Hospital, Edinburgh, and by the Edinburgh Public Health Department. It is based on the average of a large series of weight charts of the hospital class of patient. A weight chart for premature infants is not given in text-books but Hess (1923) said that seventeen infants, of which two were not breast fed, weighed $1\frac{3}{4}$-$4\frac{1}{2}$ lbs., and they gained $\frac{3}{4}$-9 ozs. in the first week of life. He also states that infants with an initial weight of 3.10-3.15 lbs.* should double their weight in ten weeks, treble it in twenty-four weeks and quadruple it in thirty-three weeks. Camerer (1909) reviewed ten premature infants weighing 2.15-4.4 lbs.* Their progress during the first four months of life is charted. For comparison the weight progress of infants under $4\frac{1}{2}$ lbs. which were collected at the Child Welfare Centres, Edinburgh, is also given.

* Weight in lbs. and ozs.

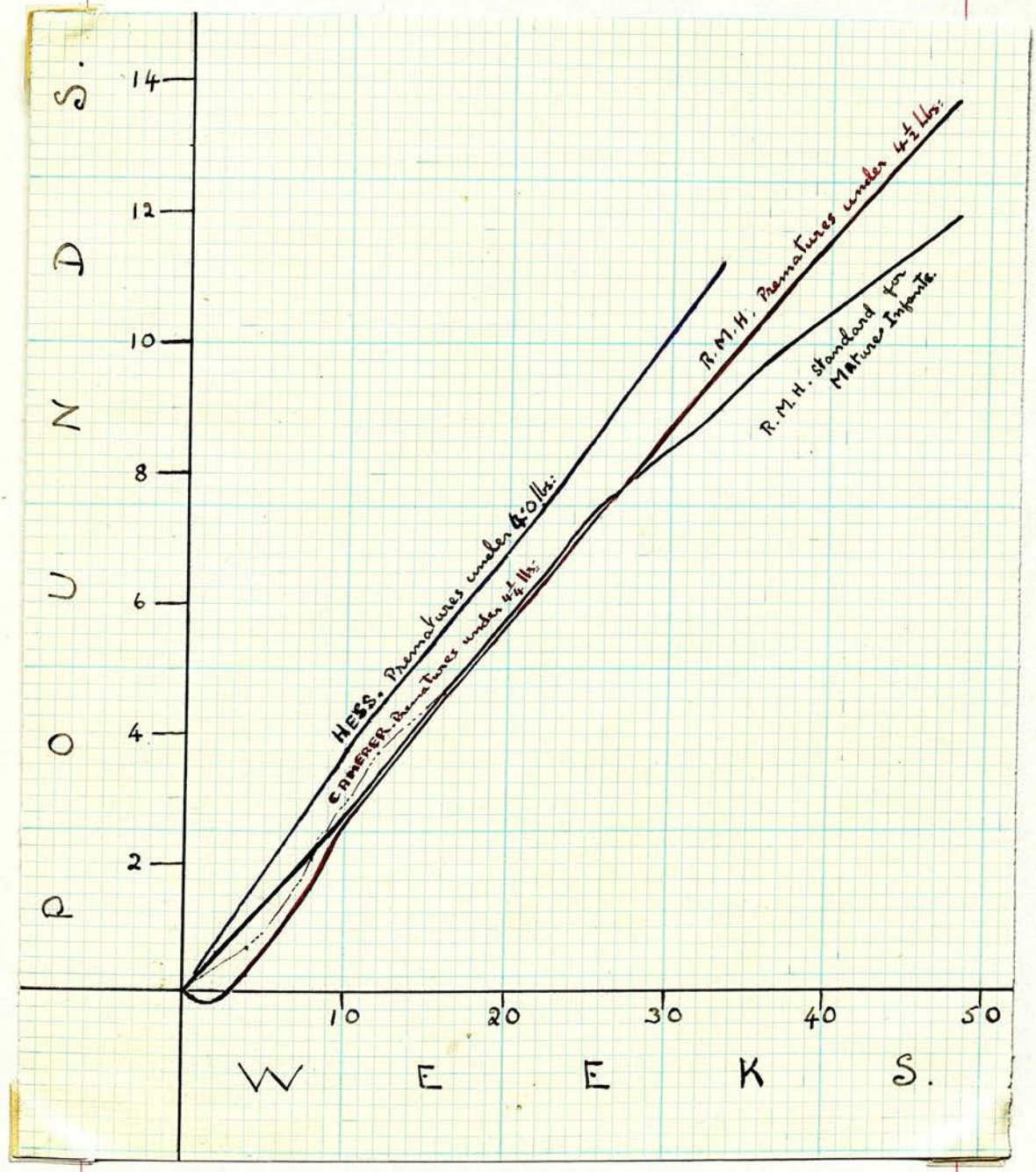
TABLE OF GRAPHS.

WEEKS.	R.M.H. standard for $7\frac{1}{4}$lb. infant.	HESS 1923 3.10-3.15.	CAMERER 1909 $2\frac{3}{4}$-$4\frac{1}{4}$lbs.	R.M.H. Infant under 4.9 lbs.	R.M.H. Cases.
2	0.10* lbs.	- lbs.*	- lbs.*	-0.$2\frac{1}{3}$ lbs.*	65
4	1.2	-	0.11	0.$4\frac{1}{3}$	61
8	2.3	-	2.2	1.$10\frac{1}{8}$	53
10	2.12	3.12	-	2.9	50
12	3.6	-	3.11	3.5	50
16	4.10	-	4.10	-	-
22	6.6	7.8	-	-	-
24	7.2	-	-	6.15 $\frac{2}{3}$	50
33	9.0	11.4	-	-	-
36	9.12	-	-	10.$7\frac{1}{2}$	28
48	12.0	-	-	13.$11\frac{1}{2}$	14

* WEIGHTS IN Lbs: AND Ozs:

77.

GRAPH TO SHOW THE PROGRESSIVE GAIN IN WEIGHT OF THE PREMATURE INFANT FROM BIRTH.



The Progress of the Premature Infant Demonstrated by the Royal Maternity Hospital Statistics.

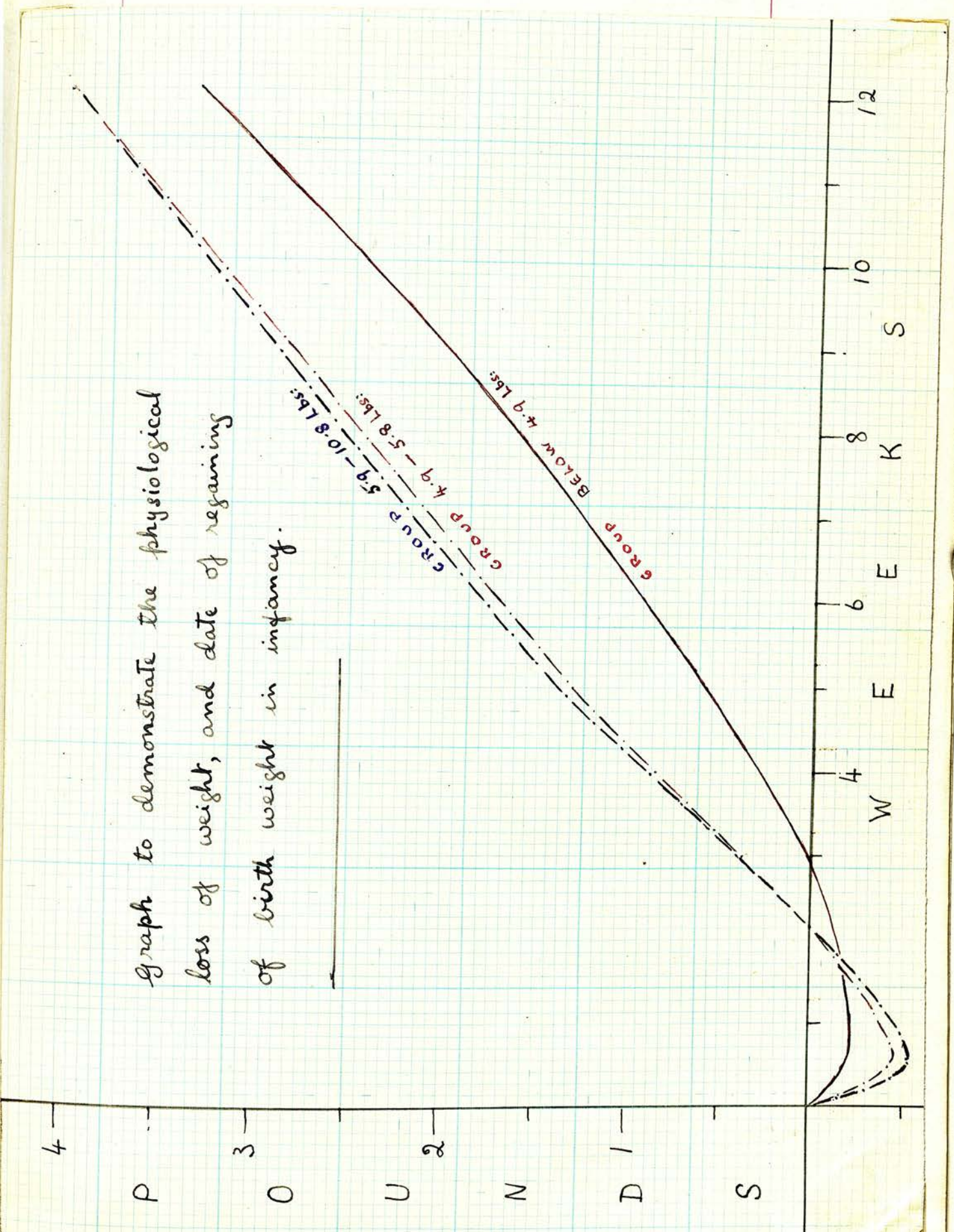
The graphs constructed for this purpose represent all the healthy premature infants born in the Royal Maternity Hospital, Edinburgh during the years 1931-1937 inclusive. All those suffering from congenital deformities were excluded. Any infant suffering from infection of the skin, respiratory tract, alimentary tract or urinary tract, as well as those with cerebral injuries and hepatic insufficiency were discounted. For controls 200 consecutive healthy and mature infants were selected. During the first 2-3 weeks of life in hospital all these infants were cared for by the same nursing staff and were fed on breast milk. After being discharged from hospital the majority of the cases attended the Child Welfare Centre, Edinburgh where their feeds were in some instances changed to an artificial one. Their general health during this period could not always be accounted for so that this portion of the graph could not be such a true representation of the normal breast fed premature infant.

The /

FIGURES TO DEMONSTRATE THE WEIGHT PROGRESS OF THE PREMATURE INFANT AS COMPARED WITH THE MATURE. FROM BIRTH TO THREE MONTHS OLD.

Weight in lbs.	Day of max.loss.	No. of cases.	Max.Wt. loss in ozs.	No. of cases.	Wt. at 3 weeks.	No. of cases.	Wt. at 5 weeks.	No.of Cases.	Wt. at 8 wks.	No.of Cases.	Wt. at 12 wks.	No. of Cases.
5.9-10.8 *	4.0	200	$8\frac{1}{2}$	200	$6\frac{5}{8}$ozs.	207	$1.6\frac{1}{4}$lbs. *	132	2.9lbs. *	127	$4.0\frac{1}{3}$lbs. *	100
4.9-5.8	4.3	162	$7\frac{1}{4}$	162	6 ozs.	65	1.5 lbs.	61	$2.7\frac{1}{2}$lbs.	60	$4.0\frac{1}{2}$lbs.	59
under 4.8	5.5	73	$3\frac{4}{5}$	73	$\frac{1}{3}$ oz.	65	$0.9\frac{1}{2}$ lbs.	61	$1.10\frac{1}{8}$lb.	53	3.5 lbs.	50

* WEIGHTS IN Lbs AND Ozs:


Graph to demonstrate the physiological loss of weight, and date of regaining of birth weight in infancy.
GROUP
BELOW 4.9 LBS:
GROUP
4.9 – 5.8 LBS:
GROUP
5.9 – 10.8 LBS:
P O U N D S
1
2
3
4
4
6
8
10
12
W E E K S

The Physiological Loss of Weight.

The maximum weight loss at birth varies within wide limits; in the mature healthy infant the loss may amount to one pound, while in the premature infant it may amount to 11 ozs. The day on which the maximum loss occurs is 1-7 days in the mature infant, and may be as late as the eighteenth day in the case of the premature infant. (See Page 81).

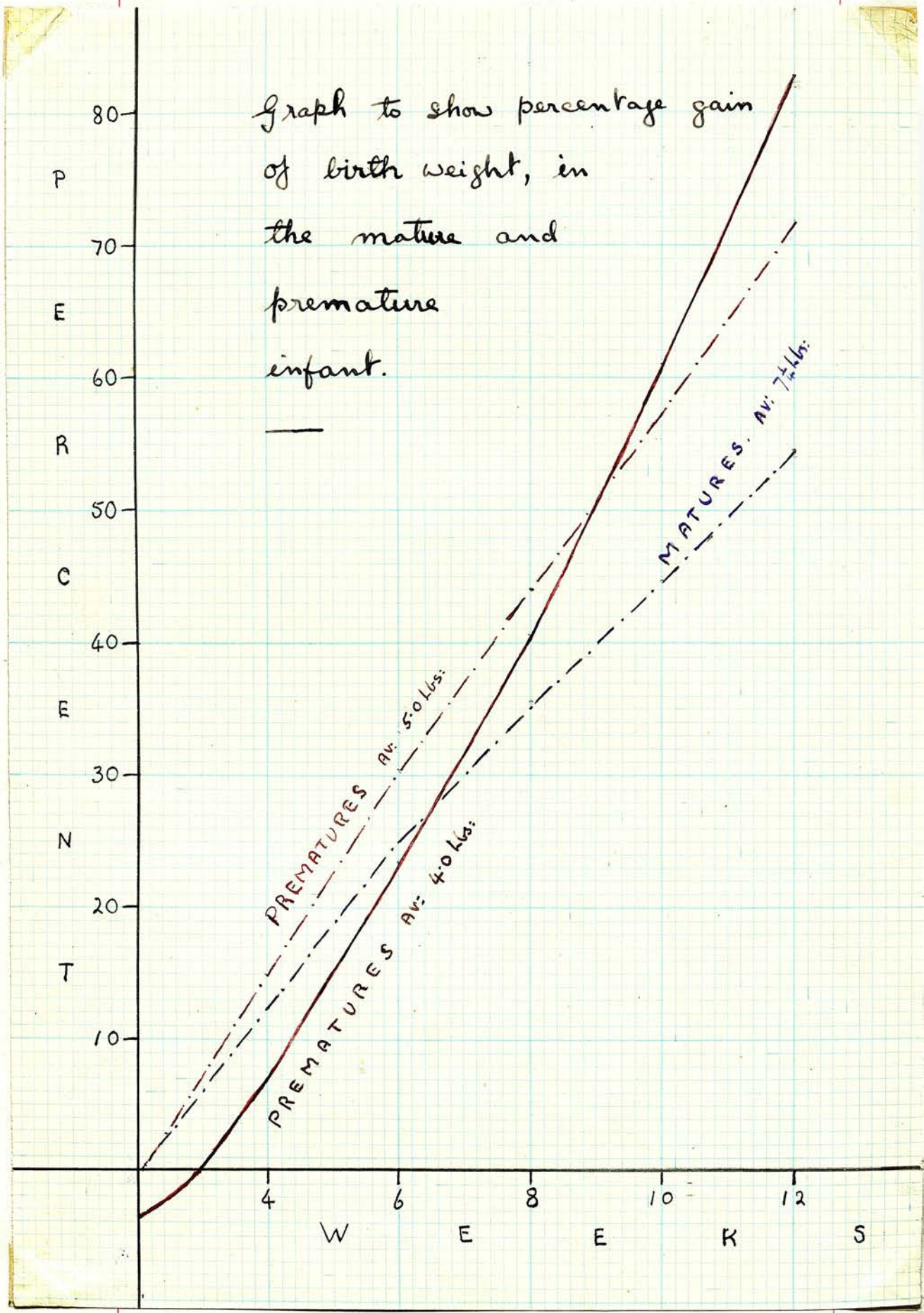
Table of the Physiological Loss Expressed as a per cent. of body weight.

Wt. Group *	No. of Cases.	Av. Max. Loss.	Per cent. of Body weight.
5.9-10.8 lbs.	200	8½ ozs.	7.3
5.8 lb. & under.	209	6	9.0
4.9-5.9 lbs.	143	7	9.0
4.8 lb. & under.	66	3	6.0

The Date of Regain of Birth Weight.

Infants weighing over 4½ lbs. regain their birth weight on the average by the fifteenth day of life, while /

* Weight in lbs. and ozs.


Graph to show percentage gain of birth weight, in the mature and premature infant.
PERCENT
80
70
60
50
40
30
20
10
PREMATURES Av: 5·0 Lbs:
PREMATURES Av: 4·0 Lbs:
MATURES. Av: 7¼ Lbs:
4
6
8
10
12
WEEKS

while those under that weight took twenty days. In extreme cases the apparently healthy premature infant may require thirty-eight days. (See Page 81). The per centage of infants regaining their birth weight by the tenth day will now be given for comparison with those of authors already mentioned.

Cases.	Weight. Lb. Oz.	Per cent. Regain of Birth Weight.
210	5.9 - 10.5	40
108	5.1 - 5.8	40
43	4.9 - 5.0	30
37	4.1 - 4.8	30
27	3.9 - 4.0	30
12	under 3.9	0

This table was prepared from statistics collected at the Royal Maternity Hospital, Edinburgh.

The Progressive Gain in Weight.

This is clearly demonstrated in the preceding graphs in this chapter but the gain expressed as a per centage of the body weight in various weight groups gives a clearer conception of the rate of weight gain.(see opposite).

SUMMARY /

SUMMARY AND CONCLUSION ON THE GROWTH OF THE PREMATURE INFANT.

The observations made at the Royal Maternity Hospital on the growth of the infant will be compared with facts given by the authors and, finally, points of interest will be discussed.

The Maximum Physiological Loss. The loss as given in the literature is 7.5-9.5 per cent of the body weight in the mature infant, and as 7.3 per cent by the Royal Maternity Hospital statistics. With regard to the premature infants, they lose 9.0 per cent of their body weight but those under 4½ lbs. only lose 6.0 per cent. On the other hand, authors give 7.0 per cent for infants under 4.11 lbs. Therefore, the average Royal Maternity Hospital figure for all premature infants supports the statement made by authors, that premature infants have a relatively greater physiolgoical loss of weight than the full term infant.

The Day of Maximum Physiological Loss. In the mature infant it occurs on the average of 3-6 days after birth. This is in keeping with the Royal Maternity Hospital charts which show the fourth day for the maximum /

maximum loss. In contrast to this the premature infant shows its maximum physiological loss 4½-5½ days after birth,-Royal Maternity Hospital statistics.

Date of Regaining of Birth Weight. By the literature mature infants regain their birth weight 7-12 days after birth. One author merely says that only twenty-five per cent regain their birth weight by the tenth day. The Royal Maternity Hospital figures, however, give the fifteenth day for the recovery of birth weight and show that forty per cent should have achieved it by the tenth day of life. The failure of these figures to approximate one another can be explained by the type of mother feeding the infant, or the type of artificial food being used, etc. With regard to the premature infant, the regaining of birth weight may take 20-30 days according to books, but the Royal Maternity Hospital figures show that the infants, even when apparently healthy, may require thirty-eight days in extreme cases, but that they normally regain their weight by the fifteenth day if they have an initial weight of 4½-5½ lbs., or in twenty and a half days when they weigh under 4½ lbs at birth.

Progressive Gain in Weight. In reviewing the figures for premature infants as quoted by Hess it is evident /

evident that they are not supported by the detail of the number of cases examined, and that in comparison with other charts of premature and mature infants he undoubtedly over estimates the ability of premature infants to gain weight. The only criticism of Camerer's figures is that, although they compare more favourably with those of the Royal Maternity Hospital, they are based on only ten cases. The Royal Maternity Hospital graphs which are based on a relatively large number of cases probably give a fairly accurate picture of the progress of the premature infant. There are two points of interest that arise.

1. The general belief that the premature infant's progress is inferior to that of the mature infant during the first few months of infancy is a misconception. The graph showing the relative weight gain proves that the premature infant of 4½-5½ lbs. progresses more rapidly than the mature infant, while the infants weighing 4½ lbs, or less, only lag behind the heavier infants in their weight progress for the first three weeks of life. After this period the rate of gain is slightly greater in the prematures.

By /

By the beginning of the fifth week the rate of progress is further increased so that the infant is actually catching up on the weight of the mature [illegible] after six weeks and two to three days. The explanation of the retardation of growth in the very small infant is probably due to either the inadequate digestive powers, (Hess 1923) or to the subnormal basal metabolic rate during the first eight weeks of life, (Gordon and Levin 1936) or to a combination of these factors.

2. The time required for the premature infant to attain the weight of a mature infant of a comparable age varies from about 3-18 months, depending upon the degree of immaturity of the infant at birth. This is accomplished by:-

(A) A relatively greater rate of gain in weight.

(B) The mature infant declining in its rate of weight progress, while the premature infant maintains its relatively high rate of gain in body weight. This is noticeable after the twenty-sixth week of life.

CHAPTER VI.

THE CARE OF THE PREMATURE INFANT.

Countless methods of feeding the premature infant are on record, but none is universally accepted. An attempt to suggest a standard diet will be made as it is a wellknown fact that rational feeding is an important prophylactic measure for the maintenance of health. (Reuss 1931). With regard to general nursing, points of particular importance for the premature infant will be given. If the suggestions are adopted one must not hope for a reduction in infant mortality during the first few days of life, for Tow (1939) showed that past improvements in nursing technique, as well as in feeding methods, did not result in fall in the mortality rate during the first two days of life when 85 per cent of the deaths occur.

The Caloric requirements are extremely difficult to determine in infancy. It has been shown that the younger or more premature an infant is the greater is the error. (Jauregnay 1935). For the determination many methods are in use and all authors are in accord that the results of the metabolic /

metabolic rate of premature infants when referred to body-weight is similar to that of full term infants of a comparable age. When referred to body surface the rate is lower in the premature infant. This may be explained either by their larger surface areas in proportion to their weight or by the assumption that there is an inherent defect in the heat production. In conclusion, statistical analysis of basal metabolic rate of the premature infant supports either the reference to body weight, or surface area as being a reliable constant. (Gordon and Levin 1936). The recent records on the caloric requirements of the premature and mature infant will now be given:-

Schadow (1932) noted the basal metabolism of the premature infant to be lower than that of the normal infant. It is from -10 to -26.6, that is, 30-40 per cent subnormal in the first month. In the second month it is -4 to -23.8 or 19-38.8 per cent subnormal. In the third month it is -15.1 to 4, consequently the caloric requirements are 100-120 per Kilog body weight per day.

Gordon and Levin (1936) investigated twenty-two premature infants, weighing $2\frac{1}{2}$-$8\frac{3}{8}$ lbs., and 1.70 days old. They required fifty-eight Cals. per kilogram body /

body weight per twenty-four hours. These figures were less than that obtained for the mature infant of the same post-natal age.

Janet and Bocket (1933) showed the metabolism of the mature infant behaved quite differently, in that in the hundred cases they investigated there was no alteration of the rate of metabolism after the first month of life, until the infants weighed 10 kilog. At this point the metabolism began to fall.

The explanation of the abnormally low basal metabolic rate in the immature child during the first two months of life is based on (1) the giving of a submaintenance diet, and (2) the infant requiring time to adjust itself to the absence of the completely surrounding warm medium in utero in which the caloric requirements are much less than in the environment after birth. After the third month the basal metabolic rate is raised, this is supposed to be due to the increased muscular activity. (Schadow 1932).

In practice the calories necessary or recommended for a very small infant each day are 150-200 (Thursfield and Paterson 1936): 65-120 per pound body weight (Brown in Parsons and Barling 1933): 50 per pound body weight (Tallerman in Parsons and Barling 1933). and Pritchard (1938). The latter added that the figure may be /

be raised to a maximum of 70 in special circumstances, but he thought 60 was a much safer figure. This modern view is probably correct, for clinical experience proves that infants thrive as well on the relatively low caloric diet as on the excessively high ones. The reason for the higher values than those calculated by the basal metabolic rate is that the latter does not take into account all the requirements for (A) dissipation of energy; (B) Development of new cells: (C) Cell proliferation: (D) Storage of calories: (E) Momentum.

In the adult the growth factor is at its minimum, therefore the caloric requirements are relatively less per pound body weight than in the infant. (Cleveland 1938). In concluding, recent authors believe that it is more satisfactory to aim at a slow gain in weight than to try and force progress. In fact, during the first two or three weeks of life the calculated caloric and fluid requirements cannot be attained. Frequently, the very premature infant can only manage 25-30 calories per pound body weight for the first ten days of life. (Tallerman in Parsons and Barling 1933). Having grasped the approximate caloric requirements, one should /

should be guided by the reaction of the infant to the diet given. If the weight progress simulates that already demonstrated in the preceding graph there should be no dissatisfaction. On the other hand, if the weight progress deviates from the standard* the calories may be increased or even reduced. The reduction of calories is advised in the over-fed, for under such circumstances infection is likely to supervene. Besides, excessive rates of weight gain in infancy are followed by corresponding delays in growth. They, in addition, tend to increase loss and waste of energy. (Cleveland 1938).

The constituents of the diet of the premature infant may be divided into those which are capable of producing energy, and those which are not. The latter consists of salts and vitamins which are present in adequate quantities in fresh milk feeds as supplied to the average infant. In the premature infant the supply is in some cases inadequate. This is due to the fact that they lack the opportunity of storing up reserves of these elements during the eighth and ninth months of intrauterine life. It is, therefore, advisable to supply vitamins daily in the form of 'Adexolin.' /

* PAGE 81.

'Adexolin' or 'Radiostoleum', and iron in the form of iron ammonium citrate. The main constituents of the diet will be discussed under individual headings:-

Protein. It is the most important constituent of breast milk as it is necessary for tissue repair, growth and development. The daily allowance amounts to 3-4 Gms. per kilog. body weight. The advantages of a high protein diet, e.g., 4 Gms. per kilog. body weight are:- (1) Clinically it is well tolerated in very young infants in spite of pepsin and probably trypsin and erepsin, being subnormal in quantity during the first three months of life. For example, colostrum, which is supposed to be beneficial to the newborn, contains 6.8 per cent and in extreme cases 15 per cent protein. (Sheldon 1936 and Abt 1923). (2) A striking gain in weight follows an increase of protein in the diet such as 4 Gms. per kilog. per lb. body weight. Not only do normal children benefit, but the undernourished shows even a greater improvement. (Hawks et alia 1928). This is further supported by the fact that the high protein content of cows' milk is necessary for the rapid rate of growth of the calf. (3) The specific dynamic action has the power of raising the basal metabolic rate in infants /

infants or children. In most instances it can be brought from subnormal levels to normal in the child. Only slight increases beyond normal are evident although such increases calculated on the bases of surface area of the body are possible with a high protein diet. The maximum elevation of metabolism is produced by a high caloric and high protein diet. (Johnston 1936). The dynamic action has been shown to be present two hours after a feed of milk plus protein in infants 2-3 months old, and that its effect remained unchecked at the end of six hours. (Levin et alia 1927). Protein may be supplied to an infant as:-

	Casein.	Lactalbumin.	Total per cent.
Human milk	1	2	1.25
Cows milk	3-5	1	3.5
Colostrum			8.6
Casec or Protosol	1		88

(Sheldon 1936).

The breast milk protein contains the kind and the amount of amino acids best suited to the infant. With it the infant's rate of growth is superior and its gastric and intestinal digestion more rapid and efficient owing to the lack of buffer action of the protein /

protein and to the formation of a flocculent soft curd. On the other hand, the cow's milk protein has a strong buffer action and gives rise to the formation of a firm tough curd in the stomach. (Nicholson 1931). The author also believes that it is necessary to give twice the amount of cow's milk protein as compared to that of human milk in order to supply the essential amino acids.

The gross difference in the chemical composition of human and cow milk results from their adaptation to the different rates of growth of the human and bovine young. The greater richness of the protein and minerals (tissue building substances) of the cow's milk makes it the natural food for a young animal which doubles its weight in 47 days, (the human requires 120 days). (Pfaundler and Schlossmann 1935). Lastly, Protosol has been mentioned as it is exceptionally useful in the preparation of the high protein diet. A ½-1 drachm of the preparation is added to 3 ozs. of the milk mixture to raise the protein content 2⅓-4⅔ calories per ounze. This is sufficient to test whether the infant will yield to the treatment.

Fat /

Fat Requirements. It constitutes between 28-38 per cent of the total caloric intake, depending on whether half or full cream milk is given. The minimum amount is desirable for the young, weakly or ill infant, but in so doing, the total caloric requirements as well as the correct proportions of protein and fat must not be sacrificed. It should be remembered that fat is the chief source of vitamins A and D, and that if small amounts of fat are given, or milk in which the vitamins have been destroyed completely or partly, additional vitamins in the form of codliver oil, haliverol, adexoline, etc., must be supplied. The low fat tolerance is accounted for by:-

1. Lipolitic ferments are subnormal in quantity and in activity in the young newborn mature infant, and even to a greater extent in the premature infant.
2. Retards gastric digestion.
3. Fat absorption has been shown to be exceptionally poor in premature infants and in twins. (Tidwell et alia 1937).

These authors also noted that premature infants, twins and marasmic children absorbed olive oil and soybean oil far more completely than butter fat, and if they are substituted for it, the improvement in nutrition is often promptly reflected in the infant's weight curve.

Carbohydrate. It forms 50 per cent of the total caloric intake, and is supplied chiefly as disaccharides, lactose and sucrose, which are well tolerated. This is confirmed by the fact that infants have a respiratory quotient of 0.88 during the first week of life. (Gordon and Levin 1936). In fact it is remarkable how well the premature or marasmic infant, or even the normal infant, reacts to Nestles Condensed Milk with the following formula:-

P. 8.95% F. 9.9% Milk sugar 12.19%
Cane sugar 40.54%

In certain cases some infants which do not thrive on other feeds, including breast milk, immediately put on weight with the Nestles Milk. Some paediatricians suggest that it is not only the high carbohydrate content but also the low protein. This, however, is not convincing as protein has been shown to be beneficial even to the undernourished. Again the high carbohydrate intake does not raise the caloric value, therefore the beneficial effect must be due to the fact that the infant can only metabolise a certain quantity of lactose, and additional carbohydrate must be supplied in another digestible form, in this instance "cane sugar." This argument is further /

further supported by the investigations on digestive ferments which showed that maltase is deficient in premature infants. Starch is a form of carbohydrate that is not acceptable to the infant under six months of age owing to the infant's deficiency of the necessary ferments, ptyalin and amylase.

In concluding, a feed containing 7.5 per cent sugar is ideal for the normal healthy infant, but for the weakly infant or premature infant under four and a half pounds a feed containing 12 per cent carbohydrate is not excessive. This is best done by adding sucrose to the milk. Even larger amounts may be added with safety for in the Universitates Kindeklink, Vienne, 12½ per cent sugar is added to all feeds given to premature infants. (Emdin 1928).

Water Intake. The daily fluid intake of the infant at term is 2½ ozs. per lb. body weight. For the premature infant 3 ozs. per lb. is most frequently supplied, but the reaction of the child to the quantities given should be the best guide as to whether the feeding is correct. If deficient fluid is given (1) dehydration fever may appear. This is most commonly seen about two to four days after birth: (2) dyspepsia due to concentrated protein may occur. This is due to the formation of the tough casein curd /

curd of cow's milk.

If excess fluid is given (1) gastric distension followed by vomiting may occur. (2) Gastric distension followed by distressing symptoms such as respiration, embarrassment, apnoea, and even death may occur. The mechanism of these symptoms has created much controversy. Apnoea is reviewed by Raiha and Salmi (1934). They gave numerous theories, but failed to come to any definite conclusion.

(A) Incomplete expansion of the pulmonary alveoli. Ylppo conceded only a minor rôle to this factor and emphasised the importance of B.

(B) The abnormally acid reaction of the blood and tissue of premature infants.

(C) Over parasympathetic stimulation.

(D) Alkalosis following the gastric secretion.

(E) Mechanical inefficiency and physical weakness of the thorax in the immature infant.

(F) Under development of the regulating function of the central nervous system.

(G) The concentration of the haemoglobin has been noted to be subnormal in such cases, and as it gradually returns to the normal level the breathing becomes regular.

(H) /

(H) Cerebral haemorrhage accounts for some cases. Owing to the possibility of these symptoms being due to over distension of the stomach a knowledge of the capacity of the stomach at various stages of maturity along with the rate of expansion after birth will be given. Hess (1923) quotes Pritchard's figures who measured the capacity by filling the stomach with water at 15 cm. water pressure.

Weeks Gestation.	Drachms.	Minims.	CC.
24	1	7	5
26	2	18	8
28	2	49	9.9
32	5	4	18
36	7	2	25
40	12	40	45

Emdin (1928) gives 2-5 c.c. for the stomach capacity of a 2 lb. infant. These figures are only approximately correct, whether estimated in the living subject or at autopsy. The variations are due to (1) the varying elasticity of the stomach in life and after death; (2) Gastric residue may be present before or after making the estimations; (3) Fluid used /

used in the living subject for the determinations is liable to pass partly through the pylorus as soon as it enters the stomach. Nevertheless, the results are sufficient to prove the importance of giving small feeds to the premature infant. With age the stomach capacity rapidly increases as shown by the following Table given by Holt (1911) who measured the stomach capacities at post-mortem:-

Age.	No. of cases.	Average stomach capacity.
Birth	5	36 cc.
2 weeks	7	45 cc.
4 weeks	4	60 cc.

Tow (1937) also estimated the stomach capacity to be ½-3 ozs. in the first week of life, and 4-5 ozs. at the end of the third week. Thus, the following Table for feeding a food of 20 Cals. to the oz. is given by Pritchard:-

Day.	Drachms per feed.	Drachms per day.
1	1	6
2	2	12
3	4	24
4	6	36
5	8	48
6	10	60

Daily /

Daily increments of 2 drachms is continued until the estimated requirements are obtained. If signs of over feeding or such symptoms as diarrhoea and vomiting appear, either reduction of the feeds or temporary cessation of daily increments should occur. In cases where inadequate fluid can be given by mouth it may be necessary to give it subcutaneously, or even intravenously, if the infant is in a grave condition. Rectal administration is not advisable. When the fluid intake is subnormal the daily caloric requirements may also be reduced to subnormal limits, but concentrated feeds may be tried. Webb (1934) states that they are very well tolerated. The type of mixture given may have 17 per cent sugar added to the normal feed.

Number of Feeds. Feeding should be commenced about 6-8 hours after birth as acute inanition readily develops in the premature infant. The feeds for the first twenty-four hours should be six hourly and consist of 1-2 drachms of 5-10 per cent glucose in saline provided colostrum is unobtainable. After this period the feeding is best to be three hourly even in the premature infant for their digestion and absorption is slower than in a full-term /

full-term infant. (Pritchard 1938). There are times when two hourly feeding is essential, for example, if the infant takes exceptionally small quantities at a feed it is necessary to feed it more frequently in order to supply the daily requirements. Saxl (1937) says that any infant weighing less than 4 lbs. should automatically be given two hourly feeds during the day, and three hourly at night, yet for those under 3 lbs. he advocates three hourly feeds during the day and four hourly at night. These views are, to some extent, perplexing, but probably harmless to the infant, for it has been shown by Taylor (1917) that the emptying time for the stomach in the premature infant under one month of age was 1 hour 40 minutes, while in the full-time infant from 2 weeks to 4 months old it was 3 hours 40 minutes. This was judged by the appearance of hunger contractions of the stomach as he found that they were reflexly inhibited by the presence of food in the stomach in infants of any age. Moritz and Schmitt (1933) had similar results for the premature infant, the stomach emptying time being 1 or $1\frac{1}{2}$ to 2 hours. In concluding, three hourly /

hourly feeds are recommended when giving six or more feeds per day. If only five feeds are given daily four hourly feeding is recommended. The following Table indicating approximately the number of feeds per day for various sized infants is given:-

Feeds per day.	Weight of infant.
5	over 7 lbs.
6	6-7 "
7	5-6 "
8	under 5 "

There is, however, no set rule, feeding depends upon the general development in relation to digestion and the ability to retain the food as well as upon the attendant feeding complications such as gastric distension, cyanosis and asphyxia.

Types of Food for the Premature Infant.

Breast Milk. It is generally accepted that the mother's milk is the ideal food for the mature or immature infant. (Waddell et alia 1937; Parsons and Barling 1933; Sheldon 1936; Thursfield and Paterson 1934; Saxl 1937; Paterson and Smith 1938; Pritchard /

Pritchard 1938). Pritchard and Saxl also emphasise that it is even more important for the premature infant than for the mature infant.

The advantages of breast feeding over artificial are (A) A greater freedom from disease. (B) A greater power of recovery from disease. (C) Better rate of growth and development. The results in pyloric stenosis give straight forward evidence of this. In Newcastle Babies' Hospital the mortality in 114 breast fed infants with pyloric stenosis was 5 per cent, but in 133 bottle fed infants it was 30 per cent. The most complete evidence is to be obtained from the studies of Grulee and Sanford in Chicago. They investigated both the morbidity and mortality rates in 20,000 infants. Including every minor disturbance of health the morbidity rate in the breast fed group was 37 per cent; in the artificially fed, 63 per cent, and in the partially breast fed 53 per cent. Of their 9,749 breast fed infants only 15 died; of 1,707 artificially fed 144 died, and of 8,605 partially breast fed 59 died. (Spence 1938).

If this is true it is strange that one type of food is as useful for the abnormal infant as well as /

as for the normal. It would seem that human milk which is preferable to any other would be better to be modified for the premature infant. The modification would aim at producing a milk with a similar composition to that found during the early lactation period, and giving this to the premature infant until its weight and digestive powers were equal to that of the mature infant. With this view in mind and the necessity for producing a suitable artificial diet for all classes of infants an account will be given of the composition of human milk during the lactation period.

Colostrum is secreted during the first few days of lactation. Sheldon (1936) gave its formula as P. 8.6 per cent F. 2.3 per cent Ch. 3.2 per cent, but it is not constant, as shown by the fact that Abt (1923) stated that the protein content may reach 15 per cent. The fullest account on the subject is given by Pfaundler and Schlossmann (1935).

Colostrum post-partum.	H_2O	P.	F.	Ch.	Cals. per Litre.
28-51 hrs.	85.5	5.8	4.08	4.09)	1,100
26-60 hrs.	87	3.17	3.92	5.48)	to
Over 88 hrs.	88	2.04	2.89	5.75)	1,500
Milk		1.09	0.76	2.94)	700 to
		1.90	9.05	7.20)	750

Milk /

Milk rapidly replaces colostrum when by the eighth day it reaches its average composition. Sheldon (1936), however, said that the milk does not attain its mature proportions until the end of the first month of lactation. From this period until the end of lactation there is little alteration in the formula. The protein, fat and carbohydrate, however, are said to diminish during the course of lactation. How well these assertions represent the rule is to be doubted, for the investigations on the subject are inadequate.* The relationship between the production quota and the quality and quantity of the milk in man is not known with certainty.* During nursing the composition of milk changes.

1. The lactose content in milk was shown to vary by Novellis Di Coarazze (1936) who examined the milk of twenty mothers. The maximum figure was 8 per cent, the minimum 5.3 per cent, and a mean figure 6.55 per cent. In fifteen out of twenty cases studied the curve followed a definite trend. The lactose content would be the highest near the beginning of nursing; it would fall to reach its minimum after ten minutes, and /

* Pfaundler and Schlossmann (1935).

and then rise again to a figure not quite so high as that shown at the start of nursing. The maximum variation in the lactose content of mother's milk in a single case was approximately 1.5 per cent, although the usual variation was approximately 0.5 per cent.

2. The protein content of milk does not show any appreciable variation during nursing. Bieber (1936) came to this conclusion after testing the milk before nursing, five, ten and fifteen minutes after nursing.

3. The fat content. It is the most variable constituent of breast milk. At the midday and afternoon feeds it may be as much as 2 per cent above the amount in the early morning feed, and not only does it vary at different meals, but it also varies during nursing. The milk at the end of a feed may contain 3-4 per cent more fat than at the beginning, (Sheldon 1936), while Holt and Howland (1926) give the fat content at the commencement of nursing as 1 per cent and at the end of nursing as 7-8 per cent.

We may conclude this review on the composition of human milk that (A) a concentrated feed is a natural event during early infancy. (B) A high per centage /

centage of protein is desirable in early infancy. (C) Since the lactose content is higher at the beginning of the nursing, and fat at the end, we may presume that the former is the more digestible food and better for supplying calories for the weakly infant.

Presumably paediatricians have had these views in mind when they have modified human milk by the addition of water, sugar, protein, or even dried cows milk. Unfortunately the results of their efforts are not published, presumably because the very small infants that would most benefit by the feeds frequently suffer from ill health or die from vascular accidents or infection.

Condensed milk. It is one of the most popular artificial feeds for the premature infant. The sweetened variety may be given in a dilution of 1-12 and gradually raised to 1-4 by the end of the third week, while the unsweetened is given in about half these dilutions, and sugar is also added. On the clinical and theoretical ground it is a difficult artificial feed to better for the premature infant.

Lactic acid in whole cows milk. It is perhaps even a more /

more popular artificial feed for the premature infant. Lactic acid was advocated by Paterson and Smith (1938) who believed it should be added to dried milk as it is more digestible than raw milk. Smyth and Hurwitz (1935) came to the same conclusion after feeding 117 infants on buffered lactic acid evaporated milk and a similar number of controls. Waddell et alia (1937) merely stated that after fifteen years of experience in treating premature babies they found whole lactic acid milk to give the best results. The advantages of using lactic milk are:-

1. Infants under 6 weeks of age tolerate it well.
2. Debilitated infants are particularly benefited.
3. The initial loss of weight at birth is less.
4. The return of birth weight is sooner.
5. At the end of the hospital period there is a more substantial gain over birth weight.
6. It enables the infant to tolerate a liberal supply of fat which accounts for the gain in weight and general improvement.
7. It increases the safety level to which the sugar may be added to the feed.
8. /

8. There is less icterus neonatorum.

9. The mortality rate is reduced. (Smyth and Hurwitz 1935, Gleich 1929, and William and Kastler 1934).

These authors may over estimate the power of the lactic acid, but there is no doubt that clinically and theoretically it is a sensible type of feed for the premature infant which is not thriving. Routine administration of the feed is unnecessary and to be deprecated, for the healthy infant has been shown to have, as a rule, a gastric secretion adequate in quality. In fact, the premature infant may show hyperacidity at birth, while the mature infant shows hyperacidity in the fasting juice in 47.37 per cent of cases. Under these circumstances adding acid to the feeds would increase the acidity of the gastric contents and at the same time increase the predisposition to peptic ulcers. (Wyllie 1938).

With regard to the type of food to which lactic acid should be added, there are two trains of thought. Firstly on clinical grounds it is considered better to add it to a dried milk; secondly, since raw cows milk is better than dried cows milk it would seem theoretically more rational to add lactic acid /

acid to cow's milk when the occasion arose. The only drawback in using lactic acid feeds is to get it prepared correctly, but with a good mother or nurse there should be no difficulty in this matter.

Protein milk. Although this type of food is not so popular Parsons and Barling (1923) advocate it for premature infants. The high protein in colostrum and in milk feed is thought to be beneficial, particularly for stimulating metabolism and growth, and if lactic acid be added to the feed there would certainly be no danger of protein dyspepsia.

Simple milk dilutions. Of all the foods that have been tried in artificial feeding there is not one better than raw milk, or its simplest dilutions. (Pfaundler and Schlossmann 1935). In fact Dennet and Craig (1932) who studied the feeding of 443 infants decided that the average infant seems to gain weight as well on fresh modified cows milk as on breast milk during the first six months of life. It should be noted that premature infants are not included, but from the weight charts of these infants it is probable that premature infants weighing over $4\frac{1}{2}$ lbs. would thrive on this feed.

Peptonisation /

Peptonisation of feeds. This is seldom practised nowadays, partly because lactic acid as a milk modifier is preferable, and partly because unpredigested food is thought by some people to stimulate the primitive gastric and intestinal digestion. (Hess 1923). Also, it has been noticed that infants fed perpetually on this type of food do not thrive satisfactorily. Nevertheless, Pritchard (1938) advocates peptonised feeds for all artificially fed premature infants. The feed should be completely peptonised during the usual colostrum period, after that time peptonising may gradually be reduced to 5-10 min. daily. If this is carried out the peptonising process should reach zero point in 18-36 days.

Dilutents and Milk Modifiers.

When substances are added to milk they generally make the curd more digestible. This is brought about by reducing the concentration of the clotting constituents, calcium, renin and casein, the curd that then forms is large and soft, not hard, tough and shrunken. Other milk modifiers act directly on the one or more of the constituents of the milk.

(1) /

(1) Colloidal milk modifiers. The following substances included in this groups are mentioned in the order of their efficiency:- Sugar, barley water, banana, gelatine. They act by lowering the tension of the clot and allowing it to swell.

(2) Sodium citrate. It prevents the formation of clot by the formation of soluble sodium caseinate. Its addition to the milk is simple but its use has been largely replaced by lactic acid.

(3) Acidification of milk may be carried out by the addition of several acids; by far the most popular is lactic acid as has already been mentioned in connection with artificial feeding of the sick or premature infant. Its efficacy is due to:- (A) The production of a fine digestible curd. (B) Removal of the buffer action of the milk, thus assisting the sub-normal gastric secretion;in so doing the acidity and emptying time of the stomach approximates very closely that with breast milk feeds. (C) The acidity inhibits bacterial activity, thus preventing fermentation and diarrhoea. (D) The gastric contents on leaving the stomach is exceptionally acid. This gives a greater stimulation to the flow of secretion which, in turn, causes /

causes better biliary and pancreatic secretion. (E) It also helps solution of, and better absorption of calcium and phosphorus. (Nicholson 1931).

Further scientific explanations of the beneficial action have been sought by Brahdy (1927). He investigated the lactate ion in the blood of infants fed on lactic acid feeds, and those fed on pure milk, but he found no marked variation between the two groups. Therefore the lactate ion could in no way influence the peripheral metabolism. He finally suggested that the lactate ion may act on the complex metabolism of the liver.

(4) Predigestion of milk. Peptonisation of feeds is not advocated at the present day as infants do better, on the whole, with undigested feeds. There is, however, one partly digested feed of marked value to the under-nourished infant. It consists of milk and water to which both sugar and Benger's food are added. The mixture is allowed to stand for twenty minutes before heating in order to allow the pancreatic ferments to act on the constituents of the milk. The beneficial effect is probably not entirely due to the action of the ferments but also to other constituents present in the Benger's food.

The Method of Feeding.

The method of choice is for the infant to be put to the breast. When given the breast the infant has to work for its feed more than with artificial feeding and this in itself is beneficial to the healthy child. For the premature child,it is also recommended (Pritchard 1938), but it is important that the infant should not be allowed to tire itself out by ineffectual efforts of sucking, nor should it be left at the breast for more than ten minutes at a time. If at the end of the feed,"test-feed" proves it has had insufficient,a supplementary feed should be given with a pipette or spoon. (Pritchard 1938). This is important, as the infant if given a bottle feed will prefer it as it requires less effort to obtain its food. It should also be remembered that such feeds are better to contain no sugar as the infant will eventually prefer the sweet food to the mother's milk. The advantages of suckling are due to production of the "reflex" gastric secretion. This follows the stimulation of the mucous membrane of the mouth or by the conditioned reflexes involving the higher parts of the brain. (Starling 1936). The "visual" psychic reflex and sucking in infants has been shown to produce /

produce an increased gastric secretion both in quantity and quality. The peptic content was also greater. (Dordie 1931).

For the very weak infant artificial feeding may have to be adopted because of the inability on the part of the infant to obtain an adequate feed. The ordinary bottle feed may be resorted to but with the very feeble infant the "Belcroy" or "Breck" feeder is better. The nurse, by regulating the internal pressure of this special feeder, can deliver the milk to the infant at the necessary pressure as gauged by the ease with which the infant takes its feed.

Lastly, the feeding of those infants that are unable to suck, whether due to immaturity or injury to the brain, can be fed in one of two ways. Firstly a large medicine dropper to which has been attached a piece of soft rubber tubing may be used. Secondly, and preferably, pass a stomach tube, provided a trained nurse is available. In giving the tube feed the infant does not need to suffer any discomfort, for the very immature infant has no pharyngeal reflex, and, therefore, there is no gagging. In addition the child saves its energy. To give a tube feed a sterile nasal catheter smeared with glycerine or liquid /

liquid paraffin is passed through the mouth into the stomach, a distance of about six inches or a distance equivalent to that from the tip of the nose to the tip of the ensiform cartilage. The measured quantity of food should then be given slowly, 1½-3 min. To prevent the food from becoming mixed with air the catheter should be compressed until the feed is poured into the funnel. After the feed is given the catheter should be again compressed while it is withdrawn, in order to prevent any of its contents falling into the pharynx and being aspirated into the lungs. (Pfaundler and Schlossmann 1935).

Important Points in General Nursing.

The general nursing of the premature infant is similar to that of the mature, but points of special importance will only be mentioned.

The temperature of the premature infant is so frequently subnormal that all efforts to attempt to raise it to normal may be required. The advantage of maintaining the body temperature is revealed by experiments involving the use of the basal metabolic rate. Mordhorst (1932), with a special apparatus, which /

which permitted the varying of the temperature, noted a distinct difference between the premature and mature infant. As the temperature of the metabolism chamber was lowered it was found that metabolism of the former was increased on the average 42.7 per cent, while that of the full term debilitated infant was raised 24.3 per cent, and that of the healthy full term infant was raised 27.6 per cent. During the experiments the actual body temperature was reduced in the premature infant 0.9 degree centigrade, in the debilitated 0.6 degrees, and in the normal infant 0.4 degrees. Means for raising the temperature are:-

1. Raising the room temperature to 75 degrees Farenheit, and to 85 degrees below the bed clothes.
2. Prevention of heat loss. This is achieved by (a) not bathing the infant; (b) smearing the infant's skin with olive oil; (c) wrapping the infant in cotton-wool etc. By these means the loss of heat through water evaporation, by convection and radiation is minimised.
3. Stimulating metabolism. This is partly done by supplying /

supplying a diet with a high caloric value and a high protein content, and partly by prescribing thyroid. The dose* of the latter is 1/20 of a grain of the B.P. preparation per pound body weight or five times the amount if the fresh gland is given. Pritchard (1938) gives a quarter of the above dose and raises the dose until the temperature responds. The drug is not only of value in this respect but also encourages the infant to feed better and mature more rapidly. The death rate is said to be lowered, but the weight gain does not improve. These observations were made by Moncrieff (1938) who made his observations on twins, one of which he kept as a control.

Relative Humidity.

The relative humidity of the atmosphere is of importance as it partly controls water loss from the skin and lungs which, in turn, entails loss of calories and a fall in body weight. To keep the loss at a minimum the relative humidity of the atmosphere should be about sixty-five degrees by the wet bulb thermometer.

It must not be imagined that because of these precautions there is any disturbance in the mechanism of /

* Per day.

of loss of heat by vaporisation, for Gordon and Kelly (1936) proved by their calorimetric studies on the elimination of water through the skin and respiratory passages that the heat production of ten premature boys ranging from 3-64 days old and weighing 3-5½ lbs. was normal. The experiments were carried out under standard conditions, and the average heat lost in vaporisation represented 29 per cent of the total heat production. This closely approximates 26 per cent, the average for children and adults.

Infection.

According to authors, the premature infant is not more liable to catch infection than the mature infant, but it is far more likely to produce disastrous results. The former statement is not altogether true as achlorhydria, which is more prevalent in the premature infant, predisposes to alimentary disturbances as illustrated by cases investigated in this thesis. The latter statement is supported by Reuss (1931) who found that four-fifths of post-mortems on premature babies had signs of broncho-pneumonia. Of these three-quarters of the deaths were due primarily to the lung condition. There is no doubt that infections of other organs can produce fatal results, but the respiratory infection is the commonest, and prophylactic measures such as attendants /

attendants wearing masks when in contact with the infants should be enforced.

CHAPTER VII.

SUMMARY OF THESIS ON GASTRIC DIGESTION OF THE PREMATURE INFANT.

This thesis has been written with the view to try and clarify some of the difficulties in the feeding of premature infants, i.e., infants weighing 5½ lbs. or less at birth. For this purpose special investigations on the gastric contents and gastric mucosa have been carried out as the knowledge on the subject is deficient. For comparison a series of mature infants have also been examined.

The relation of gastric acidity to birth weight.

The methods of estimating gastric acidity in infancy have been given and criticised, errors and fallacies have also been mentioned. The method adopted was to use the fasting juice of the unfed infant. This was done in sixty-four mature infants and sixty-four premature infants, of which a proportion were abnormal, leaving only fifty-seven mature infants and fifty premature infants which could be counted as normal. Of the normal series 84.22 per cent of the mature infants had a positive Gunzberg Reaction /

Reaction, while only 54.0 per cent of the premature infants were positive. The figure for the mature infants is identical to that given by Tomotake (1930), otherwise there was no similarity to the results given by other authors. Quantitative estimations of "free" and total acidity were also carried out on these cases, provided there was at least 0.2 c.c. of fasting juice. This quantity was used for the routine micro-estimations, the details of which have been given. The results of work showed that the average "free" and total acidity in infants weighing 6 lbs. 9 ozs. to 7 lbs. 8 ozs. was 28.44 units and 71.43 units respectively. (1 unit is equivalent to 1 c.c. N/10 HCl per 100 c.c. gastric juice.) The quantity steadily diminished with the fall of the infant's weight until the "free" and total acid was only 9.42 units and 46.41 units respectively, in the group of infants weighing 4½ lbs. or less. Graphs showing the variation in the percentage of cases with hyper- and hypo-chlorhydria in the various weight groups are also given. In short, the heavier the infant was, the greater was the likelihood of hyperchlorhydria, while the lighter the infant, the greater was the chance of it having achlorhydria. At first sight these results lead one to believe that the newborn has a greater acid secreting /

secreting power than older infants or adults, but this is not true. This is illustrated by the fact that if an infant is given a test meal it invariably has a hypochlorhydria and frequently an achlorhydria. Therefore, it follows that the infant must have a highly acid gastric secretion associated with a hypo-secretion.

The practical application of the results and investigations were:-

1. The acidification of artificial or supplementary feeds of the feeble and sick infant. Its routine use for all premature infants who are not breast fed, more particularly those weighing 4½ lbs. or less.

2. Further investigations into the question of congenital achlorhydria are advocated because of the uncertainty of its existence.

3. The aetiology of peptic ulcer in the newborn and in older infants was discussed. It was considered that, in view of the recent investigations, the old theory on aetiology was incorrect, and that hyper-acidity which was the greatest predisposing factor in adults could also be applied to the newborn.

4. The use of estimating gastric acidity to differentiate haemorrhagic disease of the newborn from /

from peptic ulcer is suggested. The test was applied in two cases of melæna neonatorum, and both had no hydrochloric acid in their fasting juice, thus being in favour of the diagnosis of haemorrhagic disease of the newborn.

5. An explanation for the frequency of dyspepsia and intestinal disorders in the small infant, especially when they are over-fed, may be largely due to the stomach contents having its pH lowered for long periods at a time, thus allowing the bacterial flora to flourish and produce symptoms.

Factors influencing gastric acidity.

These were discussed and old views on their effect upon the infant agreed with the series of cases investigated, escept for those on sex. In the past the adult, and even the infant male, was supposed to have a more acid gastric secretion than the female of a comparable age, but from the fifty-three females studied at birth it was found that on the average they had a "free" acidity of 0.1-3.6 units*, and a total acidity of 5.8-9.0 units more than the fifty-two newborn males. The variation in the number of units is to allow for the infant being mature or premature.

The influence of the mother's health upon the foetus /

* 1 unit = 1 c.c. N/10 HCl per 100 c.c. gastric juice.

foetus has also been mentioned, but only briefly as there are only a few inadequate references on the subject. To these a discussion on a series of twenty-one cases has been added. It was noted that the infants of the ill mothers were in a large proportion premature, particularly when the mother had been suffering from an acute illness. The rate of progress in the infants was, on the average, slower than normal, probably more on account of the defective milk supply or artificial feeding than to the gastric digestion for their gastric secretion was only slightly impaired.

The presence of liquor amnii and bacteria in the stomach contents of the newborn was recorded because the frequency of their occurrence was unknown. Liquor was found to be absent in the hundred and twenty-eight specimens examined but, owing to the fact that most specimens were taken 6-8 hours after birth, the results must be interpreted with care. The bacteria were seen in large numbers in sixteen out of a hundred and twenty-eight specimens. They appeared more frequently in the juice of small infants than in the large, so that their presence bore a relat-tionship to the occurrence of achlorhydria. The effect /

effect of the bacteria or achlorhydria or both of them together was of no account in some cases but, in the majority, there was a retardation in the weight progress with or without diarrhoea.

The Histology of the stomach in the Newborn Infant.

The gastric digestive powers of the newborn were attacked from another angle by examining their stomachs microscopically. For this purpose the specimens had to be fixed within half an hour of death and the sections made in the usual way. It was found that if they were stained with eosin and methylene blue the oxyntic cells were most easily seen. The stomachs of six premature infants, four mature infants and two adults were examined in this way. It was discovered that the mucous membrane of infants weighing less than 4 lbs. 7 ozs. was grossly under-developed, and in appearance was similar to the foetal stomach as described by histologists. When the infants attained 4.7 lbs. the membrane was fairly well developed except for the number of oxyntic cells present. These reached their maximum number in infants weighing 6 lbs. $5\frac{1}{2}$ ozs. and over, but did not contain as many as in the adult stomach. In this series /

series of cases there was one stomach that did not fall into line with the process of development as it had an abnormally primitive mucosa. From these facts explanations of certain clinical observations were given:-

1. The weight progress of infants weighing $4\frac{1}{2}$ lbs. or less, is exceptionally slow during the first six weeks of life. This may be explained by their grossly under-developed stomach and, probably, intestine. In addition, their subnormal basal metabolic rate would also have some influence on their progress.

2. The increasing gastric acidity accompanied by the increase in birth weight up to 6 lbs. 9 ozs. is accounted for by the corresponding gradual increase in the number of oxyntic cells in the stomach.

3. The abnormal case in the series can explain the reason for an occasional apparently healthy infant not thriving as well as other infants of a comparable age.

The effect of the digestion upon the progress of the infant.

It was considered that the weight charts of infants of various birth weights was the best method of /

of recording the effect of the digestion upon the infant. Statistics for this purpose were collected at the Royal Maternity Hospital, Edinburgh. Charts given by authors for only mature infants were not so good for comparative purposes. The most striking feature of the charts was the fact that only infants born weighing 4½ lbs., or less, were exceptionally slow in gaining weight during the first six weeks of life. Their initial loss occurred a day later than in heavier infants, their return to birth weight was 20½ days after birth as compared with the 15th day in larger infants. The theory for this behaviour has already been given by the histological findings.

The care of the Premature Infant.

A discussion on the caloric requirements, the constituents of the diet, and the types of suitable food for the premature infant has been given. Diluents of feeds and milk modifiers with special reference to lactic acid feeds were considered. It was emphasised that, owing to the varying capacity of the stomach, the volume of the feed and the frequency of feeding was important. Technical points in the nursing of premature infants such as methods of feeding /

feeding, regulation of the relative humidity of the atmosphere, maintenance of body temperature, and prevention of infection have been stressed.

BIBLIOGRAPHY.

ABT. (1923). Abt's Pediatrics, 2,528.

BABBOT, JOHNSTON, HASKINS & SCHOHL. (1923). Amer. Journ. Dis. Child. 24, 475.

BECK, A.C. (1935). "Obstetrical Practice."

BELL, T.R. (1923). Quart. Journ. Med. 17, 215.

BENNETT, T.I. and RYLE, J.A. (1921). Guy's Hospital Report. 71, 286-318.

BIEBER, A. (1936). Riv. di. clin. Pediat. 34, 712.

BILLROTH, T. (1874). Untersuchengen uber die vegetationoformen von coccabacteria septica und den Anterl Welchen sie an der Enstehung und Verbreitung der accidentellen Wundkrankheiten haben. Dissert Berlin.

BLOOMFIELD, A.L. and KEEFER. (1924). Arch. Int. Med. 38, 145.

BRAHDY, - (1927). Amer. Journ. Dis. Child. 33, 451. "Lactate Metab. in Infants and its relation to lactic acid milk."

BREMER, R.L. and LEWIS, F.T. (1927). A Textbook of Histology. P. 251.

BRESLAU, - (1866). Ueber Enstehung und Bedeutung der Darmgase bei neugeborenen Kindern, Monatschr. f. Geburtsh u. Frauenkr. 28, 1.

CAMERER, - (1900). Beitrag. Zur Physiologie des Sauglingsalters Ztschr. f. Biol. 39, 37.

CAMERER, - /

CAMERER, - (1909). Med. Wehnschr. P.34.

CLEIN, Norman (1929). Amer. Journ. Dis. Child. 37, 751.

CLELAND, N.C.W. (1938). Amer. Journ. Dis. Child. 46, 675. "The motion of growth."

COHNHEIM, - (1903). Ztschr. f. Physiolog. Chem. 37, 467.

COWDRY, E.V. (1932). "Special Cytology." P.217.

CURTIS, - (1933). Obstetrics & Gynaecology. 1, 897.

DAVIDSON, - (1921). Arch. f. Kinderheilh. 69, 142-229.

DAVIES ET ALIA. (1930). Quart. Journ. Med. 24, 1-14.

DENNETT and CRAIG. (1932). Med. Journ. Record. 134, 4.

DORDI, Anna Maria (1931). Riv. di. Clin. Paediat. 29, 791.

EMDIN, - (1928). Arch. Dis. Child. 3, 262. "Vomiting in premature infants."

ESCHERICH, T. (1885). Die Darmbakter des Sauglings und des Neugeborenen. Fortschr. d. Med. 3, 275.

ESCHERICH, T. (1886). Die Darmbakterier des Sauglings und ihre Beziehung zur Physiologie der Ver-daung. Dissert. Suttgart.

FRIEDENWALD ET ALIA. (1924). Ann. Clin. Med. 22, 292.

GIAMM, G. (1934). Riv. di Clin. Pediat. 32, 676.

GLEICH, /

GLEICH, Morris (1929). Med. Journ. and Research. 130, 153.

GORDON and KELLY. (1936). Amer. Journ. Dis. Child. 52, 1100. "Respiratory Metabolism in Infancy and in Childhood."

GORDON and LEVIN. (1936). Amer. Journ. Dis. Child. 52, 810. "Basal Metab. and Respiratory Exchange in premature infants."

GORHAM, F.D. (1921). Arch. Int. Med. 27, 434.

GRADWELL, - (1938). Clinical Laboratory Methods and Diagnosis. P. 578.

GRISWALD and SCHOHL. (1925). Amer. Journ. Dis. Child. 30, 543.

GRIES, Gertrude (1931). Monatschr. f. Kinder. 49, 411.

GUNDEL, M. and SCHWARTZ, G.K.Th. (1931-32). Ztschr. f. Hygiene u. Infection-strrankhertein. 113, 411.

GUNDOBIN, - (1912). Deson der heilen des kinder-salters Berlin.

HADFIELD and GARROD. (1938). Recent Advances in Pathology. P. 246.

HALL, Ian C. and O'TOOLE, Elizabeth (1935). Amer. Journ. Dis. Child, 49, 319.

HALPERN, L.J. (1934). Jour. Paed. 5, 40.

HANKS, - (1926). Journ. Biolog. Chem. P.69.

HARRISON, G.A. (1937). "Chemical Methods in Clinical Medicine." P.425 & 434.

HAWKS, WANG, and KAUCHER. (1928). Amer. Journ. Dis. Child. 36, 1161. "Metab. of the Undermourished Child."

HELLEBRANDT /

HELLEBRANDT ET ALIA. (1935). Amer. Jour. Digest. Dis. & Nutrit. 2, 402-408.

HESS, - (1923). The premature and congenitally diseased infant. Pp.8-60.

HESS, A7 (1913). Ibid. 6, 264. Am. J. Dis. Child.

HIRSCH, - (1910). Die Physiologische Gewichtsabnahme der neugeborenen. Berlin Klin. Wehnschr.

HOLT, - (1911). Diseases of Infancy and Childhood. p, 309.

HOLT and HOWLAND. (1926). The Diseases of Infancy and Childhood. P.116.

IBRAHIM, - (1908). Verhandl. d. Deutsch. Gesellsch. f. Kinderh. Kohn.

IBRAHIM, - (1910). Ztschr. f. Physiol. Chem. 64,97.

IBRAHIM and GROSS. (1908). Jahrb. f. Kinderh. 68, 232.

JAUGREGUAY, Miguel A. (1935). Abstract from Amer. Journ. Dis. Child. 50,1010.

JANET, H. and ROCHET, - (1933). Bull. Soc. de Pediat. de Paris. 31, 359.

JOHNSTONE, R.W. (1937). "A Textbook on Midwifery." P. 237 & 53.

JOHNSTON and MARONEY. (1936). Amer. Journ. Dis. Child. 51, 1037. "Relationship of Metabolism to Dietry Intake."

KERR, FERGUSON, YOUNG and HENDRY. (1936). "Combined Textbook of Obstetrics and Gynaecology. P.70.

KLUMPP and NEALE. (1930). Amer. Journ. Dis. Child. 40, 1215.

KNEELAND /

KNEELAND, Y. (1930). Exper. Med. 51, 617.

KOPELOFF, F. (1922). Arch. Int. Med. 30, 118.

LANGSTEIN, - (1908). Jahrb. f. Kinder. 68, 9.

LEE, de - (1915). Principles and Practice of Obstetrics. Philadelphia.

LEVIN, WILSON and RIVKIN. (1927). Amer. Journ. Dis. Child. 33, 722. "Specific Dynamic Action of Food in Normal Infants."

LIM, R.K.S. (1922). Quart. Journ. Micros. Science. 66, 187. "The Gastric Mucosa."

MacADAM, Bell (1923). Quart. Journ. Med. 17, 215.

MacFATE and LEVINSON. (1937). "Clinical Laboratory Diagnosis." P.36, 57 & 615.

MacILROY, - (1936). "The Toxaemias of Pregnancy. P.10.

MAXIMOW, Alex. A. and BLOOM, W. (1938). "A Textbook of Histology." P.381.

MOENTHAL, - (1909). Arch. Pediat. 26, 761.

MOTTE, La - Handbook on Blood Chemistry.

MORDHORST, Herbert (1932). Monatschr. f. Kinder. 55, 174. "Metab. of the Premature Infant."

MORITZ, Denes Von and SCHMITT, Anne (1923). Arch. f. Kinder. 99, 23.

MULLER, C. and BAYER, W. (1934). Arch. f. Gynak. 157, 372. "Die Pneumonie des Neugeborenen."

MULLER, J. and GUTSCHMIDT, H. (1928). Arch. f. Kinder. 84, 250.

NAUJOKS, /

NAUJOKS, H. (1921). Das Vorkomnen des Bacillus Acidophilus bei Schwangeren und Gebarnden und sein Zeitlicher und Orthicher Ubergang auf den Neugeborenen. Contralbl. f. Bakt. (Abt. I.). 86, 581.

NEALE, DEITRICH and SHELBY. (1931). Amer. Journ. Dis. Child, 41, 1016.

NEUGRESCO and HERESCO. (1921). Compt. rend. Soc. de Biolog. 40, 1159.

NICHOLSON and PERCIVAL. (1931). Journ. Med. Soc. New Jersey. 28, 217. "Essentials in Infant Feeding."

NOTHMANN, - (1909). Monatschr. f. Kinderh. 8, 377.

NOTHNAGEL, H. (1881). Die normal in den Menschtichen Darmentleerungen Vorkomnenden nicdersten Organismen, Ztschr. f. Klin. Med. 3, 275.

NOVELLIS DI COARAZZE. (1936). Riv. di Clin. Paediat. 34, 1057.

OGILVIE, J.W. (1934). Arch. Dis. Child. 9, 327.

PARKS FABER, - (1937). Lect. on Int. Med. New York.

PARSONS, - (1924). Lancet 1, 797.

PARSONS, - (1929). Proc. Royal Soc. Med. 31, (2), 1043.

PARSONS and BARLING. (1933). Diseases of Infancy and Childhood. Pp.139 & 1065.

PATERSON, Donald and SMITH, J.F. (1938). Modern Methods of Feeding in Infancy and Childhood. P.129.

PATERSON, /

PATERSON, Donald (1922). Lancet, 1, 63.

PFAUNDLER, - (1916). Korpermass studien an Kinder Ztschr. f. Kinderh.

PFAUNDLER and SCHLOSSMANN. (1935). "Diseases of Children." 1, 197-198, 305 & 313. Translated by Peterman.

PIERCE ET ALIA. (1931). Journ. Clin. Investig. 60, 651-658.

PIES, - (1911). Ueber die Dauer, die Grosse und den Verlauf der Physiologischen Abnahme der Neugeborenen, Monatsch. f. Kinder. 9, 51.

POLLAND ET ALIA. (1931). Jounr. Clin. Investig. 60, 651-658.

POLLITZER, - (1921). Pedatra. 24, 253.

PRITCHARD, Eric. (1938). "The Infant." A handbook of modern treatment. P.120.

PRICE, F.W. (1937). A Textbook of the Practice of Medicine. P. 561 & 566.

RAIHA, C.E. and SALMI, T. (1924). Acta Paediat. 15, 198.

RAMSEY and ALLEY. (1918). Amer. Journ. Dis. Child. 15, 408.

REUSS, A. (1931). Wien Klin. Wehnschr. 44, 292. "Prognosis and Prophylaxis of the Premature Infant."

SAGAL ET ALIA. (1933). Ann. Int. Med. 7, (1), 76-81.

SALOMON, R. (1922-1923). Ztschr. f. Geburtsh. u. Gynak. 85, 306.

SAXL, N.T. (1937). Paediatric Dietetics. P. 84.

SCHADOW, /

SCHADOW, H. (1932). Jahrb. f. Kinderh. 136, 1. "Energy Metab. and Food Requirements of the Premature Infant."

SCHAFER, - (1938). Essentials of Histology. P.353.

SHELDON, - (1936). Diseases of Infancy and Childhood P.43-51.

SHICK, - (1916). Zur Frage der Physiologischen Korpergewichtsabnahme der Neigeborenen, Ztschr. f. Kinderh. 13, 257.

SIZYELBOWSKY, - (1892). Jahrb. f. Kinderheilh. 34, 411.

SMYTH, and HURWITZ. (1935). Journ. Amer. Med. Assoc. 105, 789. "Buffered lactic acid evapourated milk in infant feeding."

SPENCE, J.C. (1938). Brit. Med. Journ. 730.

STARLING, - (1936). Principles of Human Physiology. P.520.

STEWART, Alice (1937). Brit. Journ. Child. Diseases. 34, 1.

STEWART, C.P. and DUNLOP, D.M. (1937). "Clin. Chemistry in Practical Medicine." P.157.

TANGE, - (1906). Arch. f. d. Ges. Physiol. 65, 64.

TAYLOR, - (1917). Amer. Journ. Dis. Child. 14, 233.

TIDWELL ET ALIA. (1937). Journ. Paediat. 481-489.

THURSFIELD, PATERSON, GARROD and BATTEN. (1934). Diseases of Children. P.76.

TOMOTAKE, Izumita (1930). Jahrb. f. Kinderh. 129, 319.

TOW, /

TOW, Abraham (1937). Diseases of the Newborn. 61-65-67.

VANZANT, F.R. and ALVAREZ, W.C. (1931). Proc. Staff. Meet. Mayo Clinic. 6, 419.

VANZANT, F.R. ET ALIA. (1932). Arch. Int. Med. 44, 345.

VANZANT, F.R. ET ALIA. (1937). Anst. Journ. Digest. Dis. and Nutrit. 3, 86.

WADDELL, PURCELL and WRAY. (1937). Year Book of Paediat. by Abt. P.7.

WEBB, C.H. (1934). South. Med. Journ. 27, 608. "Concentrated feeding in the Nutrition of Premature Infants."

WHEELER, H. (1921). Arch. Int. Med. 28, 612.

WHITE, F.W. (1922). Journ. Amer. Med. Assoc. 79, 1499-1502.

WILL and PATERSON. (1926). Arch. Dis. Child. t. 232.

WILLIAMS and KASTLER. (1932). Journ. Paed. St. Louis. 134, 4.

WILLIAM and STEIMANN. (1936). Monatschr. f. Kinderh. 84, 250.

WRIGHT, Samson (1937). Applied Physiology. P.533.

WYLLIE, David. (1938). M.D. Thesis. "The Influence of certain antacids on the acidity of human gastric juice, with special reference to Magnesium Trisilicate."

YOUNG, Professor (1939). Brit. Med. Journ. P.291. "Nutrition during Pregnancy and Lactation."

ZWEIFEL, - (1874). Untersuchungen uber das Verdaungsapparat des Neugeborenen. Berlin.